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Archives of Dermatology and Syphilology

VOLUME 15 MAY, 1927 NUMBER 5

ONE THOUSAND CASES OF CONGENITAL SYPHILIS*

C. MORTON SMITH, M.D.

BOSTON

This paper is based on a review of hospital records, mostly from the outpatient department of the Massachusetts General Hospital, since 1914. The histories of 1,600 cases were looked up, 600 of which could not be included here on account of insufficient data. Retrospectively, records fail to answer certain questions easily determined in an anticipated study. No cases from private practice, but a few from the hospital ward, are included.

A majority of the patients were admitted because of some prominent acute manifestation of congenital syphilis, such as an interstitial keratitis. The group also contains other children in the families of the patients, who came at my request for examination, and treatment if necessary; it is my custom to examine as many members of a syphilitic family as possible.

For many years, I have been deeply interested in congenital syphilis and the problems it presents medically and socially, especially the group with interstitial keratitis, in which conservation of eyesight means so much to the individual in every way, and is of economic importance to the family and the state.

Until 1910 there was no concerted cooperative effort between the ophthalmologist and the syphilographer for better therapeutic results in cases of interstitial keratitis. The former was interested in the eye manifestations, but was neither trained nor equipped to carry out thorough constitutional treatment over the long period necessary to accomplish the best results in these cases, nor was he the one to investigate the condition of other members of the family.

Through the initiative of Dr. George S. Derby of the Massachusetts Eye and Ear Infirmary, an arrangement was made whereby patients with interstitial keratitis coming to either hospital would receive the local treatment in the eye clinic, and come to Dr. Post and me for the constitutional antisyphilitic treatment and the solution of family and social problems. A well organized social service department was available for both clinics and was of great help in following up the cases and arranging for uninterrupted treatment in cases in which the family

* Read before the Golden Anniversary Meeting of the American Dermatological Association, Philadelphia, May, 1926.

was unable or unwilling to meet the requirements. For the last twelve and one-half years the constitutional treatment has been carried out in the syphilis department of the Massachusetts General Hospital.

In 1917 Drs. Derby and Post reported certain phases of this work before the ophthalmologic section of the American Medical Association, and last year Drs. Carvill and Derby presented a paper before the same body, giving the therapeutic end-results as to vision and other allied data. Their summary and comparison of final results in vision in treated and untreated cases of interstitial keratitis show such overwhelming evidence of the value of treatment that any lingering doubt in the minds of ophthalmologists or others should be removed.

They show not only that final vision has been greatly improved (there were not any cases of blindness in the treated group), but also that attacks have been shortened, and that the number of relapses has been greatly reduced. Inasmuch as this paper deals with practically the same patients as those reported by Drs. Carvill and Derby, I have not attempted to obtain final vision tests of my own, which would simply duplicate their work, but with permission quote some of their results and observations.

I am in entire accord with their conclusions as to the unquestionable value of treatment, which should be given early in an attack and continued over a long period. Beneficial results are shown in four ways: (1) improved general condition of patient, as shown in an increase in height and weight as well as in color, vitality and the general sense of well being; (2) marked improvement in vision; (3) fewer relapses; (4) less severe attack if second eye becomes involved.

The following tables were prepared by Drs. Carvill and Derby.[1]

Final Vision in Three Hundred and Fifty-Seven Eyes

	Number	Per Cent
Full vision 20/15 to 20/30	155	43.4
Good vision 20/40 to 20/60	82	23
Practical vision 20/70 to 20/200	80	22.4
Fingers	29	8
Light perception	6	1.6
Nil	5	1.3

Material of Previous Table Divided Into "Treated and "Untreated" Cases

	Treated Eyes		Untreated Eyes	
	Number	Per Cent	Number	Per Cent
Full vision 20/15 to 20/30	104	58	51	28
Good vision 20/40 to 20/60	31	17	51	28
Practical vision 20/70 to 20/200	36	20	44	24
Fingers	6	3.3	23	12.8
Light perception	1	0.6	5	2.7
Nil	0	0	5	2.7
	178		179	

1. Carvill and Derby: Boston M. & S. J. **193**:403, 1925.

In the treated cases only 1 per cent were below 20/100 while in the untreated 14 or 15 per cent were 20/100 or less.

Further end-results are cited in which ninety-three of 100 patients received arsphenamine early in the attack of interstitial keratitis involving one eye. Of this group 19 per cent had not shown involvement of the other eye at periods varying from fifteen months to more than seven years. In 3.2 per cent changes developed in the choroid, but no acute inflammatory symptoms. In 2.1 per cent the attacks were extremely

Vision in the Better Eye in One Hundred and Ninety-Three Cases

	Number	Per Cent
Full vision 20/15 to 20/30	110	56
Good vision 20/40 to 20/60	43	22
Practical vision 20/70 to 20/200	32	16
Fingers	6	3
Light perception	0	0
Nil	2	1

Vision in the Better Eye—"Treated" and "Untreated" Cases

	Treated Cases		Untreated Cases	
	Number	Per Cent	Number	Per Cent
Full vision 20/15 to 20/30	74	74	36	38
Good vision 20/40 to 20/60	12	12	31	33
Practical vision 20/70 to 20/200	14	14	18	19
Fingers	0	0	6	6.4
Light perception	0	0	0	0
Nil	0	0	2	2.1

Final Vision

	Number of Eyes	Per Cent 20/20 to 25/100	Per Cent 25/100 to 20/200	Per Cent Less than 20/200
Ingersheimer	152	59.2	22	18.4
Derby	161	65	34	0
Ultroff	200	43	36	19.5
Langendorff	165	69.6	15.5	14.9
Our cases	357	75	12.5	11.2
Our treated cases	178	84.2	11.8	3.9

mild, as evidenced by the presence of a few vessels in the cornea, while in 36 per cent there was a milder and in 8.6 per cent a severer attack in the second eye, and in 30 per cent the attacks in the two eyes occurred at the same time, or overlapped, so that the duration of the attack in either eye could not be determined.

Treatment with arsphenamine in cases in which one eye only was affected has not always prevented occurrence in the other eye. The second eye is generally involved within a few weeks after the first, and the condition usually runs a shorter, lighter course, although cases

occur in which the reverse is true. The inflammation in the second eye usually responds to arsphenamine as promptly as if the patient had never before received the drug. It is my belief that the condition here is similar to symmetrical synovitis of the knee joints: both are essentially a bilateral process, although, as Mr. Clutton pointed out in describing the knee condition, as long a period as two years may elapse between the onset in one knee and the development in the other. Hutchinson also noted this many years earlier.

There are striking analogies between interstitial keratitis and the synovitis of the knees: both are expressions of congenital syphilis; both are prone to occur at about the same age; they often occur simultaneously; they are essentially bilateral, and both respond to antisyphilitic treatment. It seems likely that it is foreordained that certain cases will be unilateral and others bilateral, and that the latter are simply running their normal course when they develop at different dates. This raises the question: Can interstitial keratitis be prevented by thorough early treatment? Drs. Carvill and Derby cite clinical histories to show that treatment of *late* congenital syphilis does not prevent the occurrence of interstitial keratitis.

Arsphenamine is peculiarly valuable in the treatment of pregnant syphilitic patients. When administered early in pregnancy it changes the prognosis of the child almost completely—entirely beyond the possibility with mercury. Many such babies have been born without clinical evidence of syphilis and have continued with negative serology. However, it is wise to consider these babies as potential congenital syphilitic patients, and to keep them under observation.

It will be interesting a few years hence to note the effect, if any, in the incidence of interstitial keratitis, deafness, Hutchinsonian teeth and symmetrical synovitis produced by intensive prenatal treatment. If these manifestations are not prevented, will they be modified? Will the children be more susceptible to acquired syphilis? It seems highly probable that such early treatment may have an effect in diminishing the frequency of these developmental and nutritional defects.

The percentage of congenital syphilis in my service is abnormally high, on account of the affiliation with the Massachusetts Eye and Ear Infirmary already explained. The incidence of interstitial keratitis would be misleading; the incidence in the general eye service is quoted.[1] "In the years 1914 to 1923, inclusive, 168,489 cases were admitted to Eye and Ear Infirmary, and of these 756 were cases of interstitial keratitis, or 0.45 per cent. The incidence each year was surprisingly uniform, 0.3 per cent being the lowest and 0.5 per cent the highest which occurred in five of the ten years." These figures correspond closely with reports from other eye clinics.

Miss O. M. Lewis, social worker, in reviewing over 1,200 records, found in practically every family a history of recurrent eye trouble or a definite case of interstitial keratitis, if the family consisted of more than one child over 6 years old.

Interstitial keratitis occurs in about the same frequency in males and females, and the time of onset is practically the same in both sexes; in this my figures are essentially like those in other reports. The condition is extremely rare before the fourth year, the greatest incidence occurring just before, and the next largest group just after, puberty. There is not a marked difference in later years, males and females being attacked in practically the same frequency. Various causes of the eye inflammation are given by patients and they range from "cold" to trauma, blows from balls or other missiles being most frequent; cinders or other foreign bodies are responsible for the eye condition in the opinion of parents. Hospital figures fail to show trauma as an appreciable contributing cause. In Dr. Derby's cases only 3 per cent gave such a history. Other authorities also report such a small number of cases following injury as to eliminate this as an etiologic or even a determining factor.

Apparently, deafness is less frequently seen in congenital syphilis than formerly. It usually occurs in one of two forms: (1) as the result of inflammation extending from the throat by way of eustachian tube—gradual onset and some hope from treatment; (2) through attack of the auditory nerve—sudden onset, deafness usually total and prognosis poor.

Available facts from my records show forty-eight patients with impaired hearing due to syphilis. Carvill and Derby report 19.2 per cent in a group of 145 cases.

There is not any doubt that syphilis is one of the greatest if not the greatest destroyer of fetal life. Figures from different observers vary, but all testify to the high mortality through miscarriages, stillbirths and early infant deaths. In my group of 645 families with a total of 3,361 pregnancies, there were 470 miscarriages, 183 stillbirths and 603 early infant deaths. Of the survivors 702 are patients with interstitial keratitis or some other syphilitic manifestation.

In 1914 Post [2] reported fifty-three miscarriages and stillbirths in 168 pregnancies. Of the infants born alive, forty-four died early, and of the remaining seventy-one, thirty-two were known to have developed late lesions of syphilis. Other authors place the fetal mortality at from 30 to 60 per cent, and of those infants born alive it has been estimated that from 30 to 75 per cent meet an early death on account of their syphilis. Furthermore, a number of those infants who survive

2. Post: Boston M. & S. J. **170**:113, 1914.

the first few months of life fall easy victims to acute respiratory infections (bronchopneumonia) or gastro-intestinal disturbances (cholera-infantum). The majority of early miscarriages are probably of toxic or other cause than syphilis, but from four to four and one-half months on to full term, death of the fetus in utero, or the expulsion of a dead fetus, can usually be credited to syphilis.

The prevention of this high toll of young human life should come through the application of prophylactic measures, especially through the thorough use of arsphenamine in the early treatment of all pregnant syphilitic patients.

A routine Wassermann test should constitute a part of the examination of all pregnant women—the number of positive cases in private practice may not reach 3 per cent, while in lying-in clinics it varies from 5 per cent to as high as 35 per cent in some localities, always notably high in colored women. While the Wassermann reaction falls far short of a "test" for syphilis, it is one of the best and easiest recognized single signs or symptoms of the disease.

For several years my department at the Massachusetts General Hospital has cooperated with the Boston Lying-in Hospital to carry out antisyphilitic treatment on cases found to have a positive blood reaction. Dr. C. Guy Lane [3] reviewed the cases of pregnant women with positive Wassermann reactions referred for examination and treatment. From Dec. 21, 1921, to Aug. 15, 1924, forty-eight such patients were admitted. Twenty-three were referred before the seventh month; twenty-three were in the seventh month or later, of which six were almost at full term; one was not pregnant, and in one the duration of pregnancy was not stated. Of these forty-eight cases, thirty-two were referred from the Boston Lying-In Hospital. The distance between the hospitals is a decided obstacle to close cooperative work. This has shown up prominently since the Lying-In Hospital has removed from nearby to its present location two miles away.

The figures emphasize the need of much more efficient team work especially between my department and the prenatal clinics, as well as a general campaign of education of all potential mothers whereby they will seek medical examination and advice early in the course of pregnancy.

Is syphilis transmitted to the third generation? So far as known, there is no record of such an occurrence in this group. In all my patients with congenital syphilis who are married and have children, the latter are clinically and serologically free from evidence of such transmission. Most of the cases of third generation transmission were reported before the Wassermann reaction was available, and when definite knowledge was not procured to rule out an acquired syphilis in the marital partner.

3. Lane, C. G.: Personal communication to the author.

Should congenital syphilitic patients be allowed to marry? Medical opinions differ. In my experience I have never seen the marital partner of a congenital syphilitic patient infected with the disease, or transmission to the offspring. Interstitial keratitis may occur, or increased deafness may prove a serious handicap, and in some instances serious nervous manifestations may develop. From a medical standpoint each case should be decided on its merits. Too many happy marriages have occurred to make congenital syphilis the only determining factor in the adverse decision. Simply the presence of a positive Wassermann reaction in these late congenital syphilitic patients should not be used against them.

In my group there are 110 cases of symmetrical synovitis. In describing this condition, Mr. Clutton said that other large joints beside the knee probably were similarly affected. I have seen cases of ankles, wrists and elbows which apparently belong in this group. There was swelling of the soft parts, some pain and limitation of motion and no change in the bony structures on roentgen-ray examination, and the joints were restored to normal by antisyphilitic treatment. These cases of synovitis of the knee are still frequently diagnosed as tuberculous joints, put in plaster casts and kept in them for months or years, syphilis not being suspected until the eyes became inflamed. Symmetrical synovitis needs only prompt recognition and thorough antisyphilitic treatment in order to restore the joints to normal. Routine Wassermann and roentgen-ray examinations should always be performed in these cases.

Dental defects due to congenital syphilis are: (1) Hutchinsonian teeth; (2) six year molars—"mulberry molars"; (3) changes in lower incisors and canines, and frequently an open bite due to failure in development of the alveolar process of the upper jaw. Significant dental defects were recorded in 389 of my patients. Most patients with congenital syphilis and suggestive teeth show other stigmas of their congenital disease. It is seldom necessary to make a diagnosis in these children on one sign alone, such as dental defects, eyes or knees. The family history is always important. Scars, lesions or a positive Wassermann reaction in either parent is strong confirmatory evidence. The possibility of an unrecognized extragenital infection should not be overlooked in seeking for evidence of acquired disease in parents. A history of alcoholism in a person is strong presumptive evidence of syphilis. From its effects on pregnancies one can often tell with considerable accuracy about the time the disease was introduced into a given family, for as the infection becomes more attenuated, miscarriages and stillbirths are usually followed by living children showing stigmas of the disease; but in time the later children may closely approach the normal.

In many families, my group records more than one child with signs of congenital syphilis. Such children, though not showing any signs of active disease, should receive treatment as a preventive.

In my group there are five instances of paroxysmal hemoglobinuria, all of which, with possibly one exception, occurred in cases of congenital syphilis. One of my cases was studied and reported on by Dennie in 1915. Antisyphilitic treatment has greatly benefited the majority of the patients.

Dactylitis is not a frequent occurrence. There have been only seven cases recorded at the Massachusetts General Hospital since 1914. Of this number three were definitely proved to be of syphilitic origin. Other bony manifestations of syphilis are usually found. The multiplicity of lesions in the same hand is definitely against tuberculosis as the causal factor. Here, as in many other cases, the diagnosis of syphilis is usually not difficult, provided the possibility is considered and search made for other manifestations.

In this group, the number of late destructive ulcerating lesions of the skin and mucous membrane has been surprisingly small. The same is also true of destructive lesions of the nasal bones and septum, and the falling-in of the soft parts, which produces the characteristic deformity of syphilis, especially in the layman's mind. In reality, this deformity is of infrequent occurrence.

Scars at the corners of the mouth and on the chin, the lips and sometimes the cheeks, the result of ulcerated fissures occurring in infancy, are not infrequent. They are of considerable diagnostic value up to the age of 20, or the time when wrinkles begin to simulate these scars.

My patients were not as carefully recorded in regard to mental and nervous defects as they should have been; hence the records are lacking in various essential details. Many of the children are backward in school: some on account of poor mental development, others from the result of the physical handicap of defective sight and hearing and the time lost from school during the active stage of interstitial keratitis.

In the group of interstitial keratitis patients reported by Dr. Post in 1917, the social service worker showed that in fifty of the children of school age, a total of sixty years' schooling had been lost. It should be possible to improve this record in the future, by prompt recognition of the disease and careful, thorough treatment. Patients seldom reach the clinic before the end of a week or ten days, the average being between two and three weeks.

Probably no other single manifestation of congenital syphilis, excepting a Wassermann reaction, has been responsible for bringing so many persons under treatment for syphilis as interstitial keratitis. Practically every patient seeks medical advice sooner or later, and in this

way not only the individual is treated, but also many families are investigated and brought under medical supervision, thereby improving their health and economic value to the community.

The recognition of interstitial keratitis is not always easy, and ophthalmologists sometimes disagree on a given case, phlyctenular keratitis being the usual difficulty in diagnosis. In my cases the eye diagnoses were all made by Drs. Quackenboss and Derby (or their assistants) at the Massachusetts Eye and Ear Infirmary.

It is my belief that interstitial keratitis means congenital syphilis—that it practically never occurs as a primary condition in acquired disease but may develop secondarily in iritis, just as a secondary iritis occurs in practically all cases of interstitial keratitis.

TREATMENT

Treatment has consisted of many intravenous injections of arsphenamine (from ten to forty) or its equivalent in neoarsphenamine, and in a few patients sulpharsphenamine has been used. Slightly subnormal doses have been given in children who were physically below par. Dilation of the pupil and all local treatment was attended to by the ophthalmologists. While the patients were receiving intravenous treatment, mercury with chalk was given by mouth, as well as syrup of hydriodic acid or potassium iodide. Some of the later cases have received bismuth in place of mercury, but as yet the number is too small to permit the forming of conclusions. Some of the patients showed greater improvement when candy and sweets were withdrawn from their diets. Inunctions of mercury have been used with good effect at times, also mercury intramuscularly.

In cases in which salmon patches appeared in the cornea or in which inflammatory products were abundant, improvement followed massive doses of potassium iodide, as it does in like conditions in other organs or tissues, and this therapy was a valuable adjunct to the other remedies. The importance of good food, fresh air, tonics, hygiene, cod liver oil and a vacation in the country, as a part of the treatment of some children with interstitial keratitis, must not be overlooked.

The social worker in the clinic is a necessity. She knows the patient and the medical needs. She also visits the family and knows why certain patients come to the clinic irregularly, and attends to such minor details as lack of funds, clothing, escort, etc. She often provides a boarding place near the clinic when ward treatment is no longer necessary, and attends to innumerable important small details that contribute so greatly to success. Moreover, she keeps the doctors in both departments informed as to the social conditions and medical progress—so essential in complete cooperation.

Changes in the methods and manner of medication, as well as changes in the patient's attitude toward himself and the clinic, have been responsible in part for the larger number of clinical visits shown in tables of later years. Intravenous and intramuscular injections have largely supplanted treatment by mouth and by inunction, the former uncertain, the latter inexact. Also, social service follow-up, better clinical results and closer cooperation between the ophthalmologist and the syphilographer have each contributed its part toward all round efficiency.

How long should treatment be kept up in congenital syphilis? There is no indication for universal application. One must consider conditions present when treatment was begun: the age of the patient; what, if any, previous medication has been given, and the amount and kind; also what are the therapeutic and serologic results and present physical condition. In these cases a long continued judicious use of antisyphilitic remedies, given intermittently, is seldom a cause for regret.

The following tables of miscellaneous data are of interest.

TABLE 1.—*Physical Examination in One Thousand Cases of Congenital Syphilis, 1914-1926 Period*

Wassermann Reaction		
Positive	615	
Negative	174	
None or no record	211	
		1,000
Head		
Square	132	
Suggestive	98	
Negative	770	
		1,000
Teeth		
Hutchinsonian	224	
Suggestive	165	
Negative	611	
		1,000
Ears		
Deaf	48	
Negative	952	
		1,000
Periosteal changes in tibia	348	
Negative	652	
		1,000
Knees		
Symmetrical synovitis	110	
Negative	890	
		1,000
Interstitial keratitis	641	
Other manifestations of congenital syphilis	359	
		1,000

TABLE 2.—*Congenital Syphilis in One Hundred Consecutive Patients Under Treatment, 1914-1918 Period*

Nationality	
American	51
American colored	2
Canadian and American-Canadian	4
Italian (5) and American-Italian (10)	15
Irish-American	13
Other European and European-American	15
Total	100

TABLE 3.—*Congenital Syphilis in One Thousand Patients Entering Massachusetts General Hospital Clinics, 1914-1926 Period*

Ages	Number of Patients
Under 1 year old	107
1 to 8 years	283
9 to 14 years	318
15 to 20 years	192
21 years and older	100
Total	1,000

TABLE 4.—*Congenital Syphilis in One Hundred Consecutive Patients Under Treatment, 1914-1918 Period*

Sex	
Male	45
Female	55
Total	100

TABLE 5.—*Congenital Syphilis in One Hundred Consecutive Patients Entering Clinic During the Years from 1914 to 1918—Parents' History*

History	No. of Fathers		No. of Mothers	
Living	68		85	
Question of living	4		1	
		72		86
Dead	19		12	
Supposed dead	4		..	
		23		12
No record (unknown)	5		2	
	100		100	

TABLE 6.—*Congenital Syphilis in One Hundred Patients Entering Clinic from 1914 to 1918—Childhood and Adolescence*

Age Began School	Number of Patients
Before 5 years of age	1
From 5 to 6 years	9
From 6 to 7 years	16
From 7 to 8 years	5
Nine years	1
No school, too young (not able or no school near; one taught at home)	12
Unknown	52
Total	100
School Grade and Age	
Too young for school	11
Special class for eye saving	1
Normal (rate of eighth grade at from 14 to 15 years)	49
Two grades (backward)	9
Three grades (backward)	3
Four grades (backward)	4
Five grades (backward)	1
Ungraded	2
Through eight grades, age	1
Unable to go or no school*	5
Unknown	14
Total	100

* Two (?) attended school in other countries.

TABLE 6.—*Congenital Syphilis in ne Hundred Patients Entering Clinic from 1914 to 1918—Childhood and Adolescence—Continued*

Time Lost from School and Causes	Number of Patients
No time lost	15
Up to six months	12
Seven to twelve months	8
One to two years	9
Two to three years	4
Three to four years	2
Five years and up	3
"Much" time	8
Amount of time unknown*	28
Too young for school	11
Total	100

TABLE 7.—*Congenital Syphilis in One Hundred Consecutive Patients Entering Clinic in 1914-1918 Period—Personal History of Infancy*

Condition at Birth	No. of Patients
Normal	44
Sickly and frail	6
Unknown, no record	50
	100
Term	
Full	62
Premature	1
Unknown, no record	37
	100
Delivery	
Normal	/42
Instrumental (1 cesarean)	10
Unknown	48
	100
Feeding	
Breast (6 cases bottle or sup after 3 months)	51
Bottle (3 cases breast fed from 1 week to 2 months)	13
No record	36
	100

Teething	No. of Patients
Normal (4 carious, 1 crooked)	24
First tooth at 9 months to 1 year+.	13
First tooth at 2 years	1
No record, unknown	62
	100
Talking	
Normal	12
At 14 to 18 months	12
At 2 to 3 years	9
After 3 years	3
No record, unknown	64
	100
Walking	
Normal	15
At 14 to 18 months	12
At 2 to 3 years	8
After 3 years	5
No record, unknown	60
	100

TABLE 8.—*Summary of Clinical Attendance of Two Hundred Patients with Congenital Syphilis*

Number of Patients				
1914	1918	Total	1922	No. of Visits
54	51	105	47	1 — 10
35	34	69	18	10 — 20
7	11	18	19	20 — 30
1	3	4	9	30 — 40
2	..	2	6	40 — 70
..	..	2	1	70 — 90
1	1	..	..	90 — 100
100	100	200	100	

TABLE 9.—*Sex in Three Hundred Consecutive Cases of Congenital Syphilis*

200 patients entering Massachusetts General Hospital clinic from 1914 to 1918
100 patients entering Massachusetts General Hospital clinic 1922

	1914		1918			1922
Male	45	+	44	=	89	52
Female	55	+	56	=	111	48
					200	100

TABLE 10.—*Total Pregnancies in Five Hundred Families and Results as Tabulated* *

Still born	167
Miscarriages	397
Early deaths	278
Living children	1,681
Total pregnancies	2,523
Patients at Massachusetts General Hospital	527

Family Number	Number of Pregnancies																
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
1	⊕	+	—	—	+	..	..	..	..	..	..	..	..	..	..	..	..
2	S	S	⊕	+	+	..	..	..	..	..	..	..	..	..	..	..	..
3	M	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
4	—	M	⊕	M	S	..	..	..	..	..	..	..	..	..	..	..	..
5	S	S	—	⊕	—	+	..	..	..	..	..	..	..	..	..	..	..
6	M	⊕	S	+	+	..	..	..	..	..	..	..	..	..	..	..	..
7	+	—	⊕	—	..	..	..	..	..	..	..	..	..	..	..	..	..
8	—	—	+	⊕	+	+	..	..	..	..	..	..	..	..	..	..	..
9	⊕	+	—	+	+	+	..	..	..	..	..	..	..	..	..	..	..
10	+	+	+	S	M	⊕	S	..	..	..	..	..	..	..	..	..	..
11	+	+	+	⊕	+	+	..	..	..	..	..	..	..	..	..	..	..
12	—	⊕	S	+	+	+	..	..	..	..	..	..	..	..	..	..	..
13	+	—	+	+	—	⊕	+	+	+	+	+	+	..	..	..	..	..
14	+	+	+	S	S	⊕	—	—	—	..	..	..	..	..	..	..	..
15	—	—	⊕	—	+	+	+	..	..	..	..	..	..	..	..	..	..
16	+	+	M	S	+	+	+	+	..	..	..	..	..	..	..	..	..
17	+	—	+	S	+	M	M	M	⊕	M	M	M	M	+	..	..	..
18	⊕	—	+	..	..	..	..	..	..	..	..	..	..	..	..	..	..
19	+	+	+	+	+	—	M	M	M	+	⊕	S	..	..	..	..	..
20	+	+	+	+	+	—	+	⊕	—	..	..	..	..	..	..	..	..
21	—	+	S	+	⊕	—	—	—	..	..	..	..	..	..	..	..	..
22	+	+	—	⊕	M	+	+	..	..	..	..	..	..	..	..	..	..
23	—	⊕	—	..	..	..	..	..	..	..	..	..	..	..	..	..	..
24	—	—	—	+	⊕	..	..	..	..	..	..	..	..	..	..	..	..
25	—	—	—	—	⊕	..	..	..	..	..	..	..	..	..	..	..	..
26	+	+	⊕	M	M	+	+	+	..	..	..	..	..	..	..	..	..
27	+	—	⊕	+	..	..	..	..	..	..	..	..	..	..	..	..	..
28	⊕	+	+	+	+	+	..	..	..	..	..	..	..	..	..	..	..
29	⊕	+	M	M	M	..	..	..	..	..	..	..	..	..	..	..	..
30	+	⊕	M	M	M	..	..	..	..	..	..	..	..	..	..	..	..
31	—	M	M	M	⊕	+	+	+	..	..	..	..	..	..	..	..	..
32	+	+	+	+	+	⊕	..	..	..	..	..	..	..	..	..	..	..
33	+	—	—	—	+	+	⊕	..	..	..	..	..	..	..	..	..	..
34	—	+	+	+	—	⊕	S	+	+	+	+	..	..	..	..	..	..
35	⊕	+	+	+	+	+	+	+	+	..	..	..	..	..	..	..	..
36	+	+	M	M	M	M	+	⊕	..	..	..	..	..	..	..	..	..
37	+	+	⊕	+	..	..	..	..	..	..	..	..	..	..	..	..	..
38	+	+	M	⊕	+	..	..	..	..	..	..	..	..	..	..	..	..
39	+	⊕	+	+	M	+	+	M	..	..	..	..	..	..	..	..	..
40	M	⊕	M	M	M	+	+	+	..	..	..	..	..	..	..	..	..
41	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
42	+	+	M	—	—	—	⊕	M	+	M	M	M	M	..	..	..	..
43	+	⊕	+	+	..	..	..	..	..	..	..	..	..	..	..	..	..
44	+	⊕	—	M	..	..	..	..	..	..	..	..	..	..	..	..	..
45	M	M	M	⊕	M	M	M	⊕	S	..	..	..	..	..	..	..	..
46	⊕	S	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
47	S	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
48	+	+	+	+	⊕	—	—	—	—	—	—	—	..	..	..	..	..
49	+	+	+	+	+	⊕	—	+	..	..	..	..	..	..	..	..	..
50	⊕	—	⊕	M	..	..	..	..	..	..	..	..	..	..	..	..	..
51	—	—	M	M	⊕	+	+	+	..	..	..	..	..	..	..	..	..
52	M	M	⊕	M	M	⊕	..	..	..	..	..	..	..	..	..	..	..
53	+	M	+	+	+	M	⊕	..	..	..	..	..	..	..	..	..	..
54	S	⊕	S	+	S	+	+	S	..	..	..	..	..	..	..	..	..
55	⊕	+	+	..	..	..	..	..	..	..	..	..	..	..	..	..	..
56	S	S	⊕	—	—	—	—	..	..	..	..	..	..	..	..	..	..
57	S	S	+	—	⊕	..	..	..	..	..	..	..	..	..	..	..	..
58	—	S	S	S	⊕	+	⊕	+	+	..	..	..	..	..	..	..	..
59	⊕	+	M	..	..	..	..	..	..	..	..	..	..	..	..	..	..
60	⊕	+	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
61	+	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
62	+	⊕	+	+	..	..	..	..	..	..	..	..	..	..	..	..	..
63	—	—	—	S	S	S	+	+	⊕	+	..	..	..	..	..	..	..
64	—	+	⊕	—	+	..	..	..	..	..	..	..	..	..	..	..	..
65	+	+	⊕	+	+	+	..	..	..	..	..	..	..	..	..	..	..
66	+	+	+	⊕	—	—	S	S	—	—	—	—	—	—	—	..	..
67	+	⊕	M	+	..	..	..	..	..	..	..	..	..	..	..	..	..
68	M	+	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..
69	M	—	+	M	S	⊕	—	+	..	..	..	..	..	..	..	..	..

* S indicates still born; M, miscarriage; —, early deaths; +, living children; ⊕, patients at Massachusetts General Hospital.

TABLE 10.—*Total Pregnancies in Five Hundred Families and Results as Tabulated—Continued*

Family Number	Number of Pregnancies																
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
70	⊕	M	M	M	M	+	..	..	..	..	..	..	..	..	..	..	..
71	⊕	+	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
72	+	+	⊕	+	+	..	..	..	..	..	..	..	..	..	..	..	..
73	S	S	—	+	—	⊕	..	..	..	..	..	..	..	..	..	..	..
74	+	⊕	+	+	+	..	..	..	..	..	..	..	..	..	..	..	..
75	⊕	S	S	⊕	⊕	S	⊕	+	M	..	..	..	..	..	..	..	..
76	—	⊕	+	+	..	..	..	..	..	..	..	..	..	..	..	..	..
77	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
78	+	+	+	—	—	+	+	⊕	—	+	+	..	..	..	..	..	..
79	+	+	+	⊕	—	—	+	..	..	..	..	..	..	..	..	..	..
80	+	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
81	⊕	—	+	+	+	+	+	+	..	..	..	..	..	..	..	..	..
82	⊕	—	+	..	..	..	..	..	..	..	..	..	..	..	..	..	..
83	+	—	—	+	⊕	..	..	..	..	..	..	..	..	..	..	..	..
84	+	+	+	⊕	+	..	..	..	..	..	..	..	..	..	..	..	..
85	+	+	⊕	+	+	..	..	..	..	..	..	..	..	..	..	..	..
86	⊕	+	+	+	..	..	..	..	..	..	..	..	..	..	..	..	..
87	+	+	—	—	—	—	—	—	S	S	⊕	..	..	..	..	..	..
88	+	+	+	+	+	⊕	..	..	..	..	..	..	..	..	..	..	..
89	+	+	+	M	M	⊕	..	..	..	..	..	..	..	..	..	..	..
90	+	M	S	—	⊕	—	..	..	..	..	..	..	..	..	..	..	..
91	—	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
92	+	⊕	+	..	..	..	..	..	..	..	..	..	..	..	..	..	..
93	+	+	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..
94	M	⊕	+	+	..	..	..	..	..	..	..	..	..	..	..	..	..
95	+	⊕	+	..	..	..	..	..	..	..	..	..	..	..	..	..	..
96	S	+	S	S	+	+	⊕	+	+	..	..	..	..	..	..	..	..
97	+	+	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..
98	+	+	+	⊕	+	+	—	+	..	..	..	..	..	..	..	..	..
99	+	+	⊕	+	..	..	..	..	..	..	..	..	..	..	..	..	..
100	—	+	+	+	+	—	⊕	+	+	+	..	..	..	..	..	..	..
101	S	⊕	+	..	..	..	..	..	..	..	..	..	..	..	..	..	..
102	+	+	+	+	+	⊕	+	+	+	+	+	..	..	..	..	..	..
103	—	+	⊕	—	M	M	M	..	..	..	..	..	..	..	..	..	..
104	S	S	S	S	⊕	M	..	..	..	..	..	..	..	..	..	..	..
105	S	S	S	S	⊕	+	..	..	..	..	..	..	..	..	..	..	..
106	⊕	M	⊕	+	M	+	M	+	..	..	..	..	..	..	..	..	..
107	⊕	+	M	—	—	—	M	M	M	..	..	..	..	..	..	..	..
108	—	+	M	M	M	⊕	+	..	..	..	..	..	..	..	..	..	..
109	⊕	+	+	+	+	+	..	..	..	..	..	..	..	..	..	..	..
110	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
111	+	M	+	M	—	—	⊕	+	+	⊕	M	M	M	..	..	..	..
112	⊕	—	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
113	M	⊕	+	+	+	+	..	..	..	..	..	..	..	..	..	..	..
114	+	+	+	+	+	—	+	—	⊕	+	+	+	+	+	—	..	..
115	⊕	—	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
116	+	⊕	M	M	M	..	..	..	..	..	..	..	..	..	..	..	..
117	⊕	M	M	M	..	..	..	..	..	..	..	..	..	..	..	..	..
118	+	⊕	+	+	..	..	..	..	..	..	..	..	..	..	..	..	..
119	⊕	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
120	⊕	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
121	S	⊕	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..
122	⊕	—	S	..	..	..	..	..	..	..	..	..	..	..	..	..	..
123	+	+	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..
124	+	S	⊕	+	+	..	..	..	..	..	..	..	..	..	..	..	..
125	M	M	+	M	M	M	M	⊕	M	..	..	..	..	..	..	..	..
126	—	—	M	—	—	M	M	+	⊕	—	+	..	..	..	..	..	..
127	—	+	—	—	—	+	⊕	+	+	+	+	..	..	..	..	..	..
128	M	S	⊕	M	M	+	..	..	..	..	..	..	..	..	..	..	..
129	—	+	—	—	⊕	..	..	..	..	..	..	..	..	..	..	..	..
130	M	M	S	S	S	⊕	..	..	..	..	..	..	..	..	..	..	..
131	—	—	—	—	—	—	—	⊕	+	+	..	..	..	..	..	..	..
132	S	+	⊕	+	+	—	..	..	..	..	..	..	..	..	..	..	..
133	S	S	⊕	M	M	+	+	+	+	..	..	..	..	..	..	..	..
134	+	⊕	+	..	..	..	..	..	..	..	..	..	..	..	..	..	..
135	+	⊕	S	S	—	..	..	..	..	..	..	..	..	..	..	..	..
136	⊕	+	+	..	..	..	..	..	..	..	..	..	..	..	..	..	..
137	+	+	+	M	M	⊕	+	+	..	..	..	..	..	..	..	..	..
138	—	—	+	+	+	⊕	+	+	..	..	..	..	..	..	..	..	..
140	+	+	—	+	+	+	⊕	+	—	+	—	+	..	..	..	..	..
141	+	⊕	+	..	..	..	..	..	..	..	..	..	..	..	..	..	..
142	⊕	+	+	+	..	..	..	..	..	..	..	..	..	..	..	..	..
143	⊕	S	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
144	⊕	—	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
145	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
146	+	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
147	+	⊕	+	..	..	..	..	..	..	..	..	..	..	..	..	..	..
148	+	+	+	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..
149	+	+	+	⊕	+	—	+	..	..	..	..	..	..	..	..	..	..
150	M	S	⊕	+	—	—	..	..	..	..	..	..	..	..	..	..	..

TABLE 10.—*Total Pregnancies in Five Hundred Families and Results as Tabulated—Continued*

Family Number	Number of Pregnancies																
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
151	—	⊕	M	..	..	..	..	..	..	..	..	..	..	..	..	..	..
152	M*	M	M	S	S	S	⊕	+	..	..	..	..	..	..	..	..	..
153	⊕	—	M	—	+	M	+	M	M	+	+	..	..	..	..	..	..
154	+	⊕	+	+	+	..	..	..	..	..	..	..	..	..	..	..	..
155	—	M	M	⊕	+	+	..	..	..	..	..	..	..	..	..	..	..
156	+	+	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..
157	+	+	⊕	+	+	..	..	..	..	..	..	..	..	..	..	..	..
158	M	+	+	⊕	M	..	..	..	..	..	..	..	..	..	..	..	..
159	—	S	S	⊕	S	..	..	..	..	..	..	..	..	..	..	..	..
160	+	+	+	—	+	⊕	+	+	..	..	..	..	..	..	..	..	..
161	M	⊕	+	+	..	..	..	..	..	..	..	..	..	..	..	..	..
162	⊕	+	+	+	+	+	+	+	M	+	M	+	..	..	..	..	..
163	M	M	⊕	—	..	..	..	..	..	..	..	..	..	..	..	..	..
164	+	+	⊕	—	+	+	—	..	..	..	..	..	..	..	..	..	..
165	+	—	—	⊕	+	M	M	..	..	..	..	..	..	..	..	..	..
166	+	+	⊕	+	..	..	..	..	..	..	..	..	..	..	..	..	..
167	+	+	⊕	+	..	..	..	..	..	..	..	..	..	..	..	..	..
168	—	⊕	+	..	..	..	..	..	..	..	..	..	..	..	..	..	..
169	—	+	+	+	—	+	M	M	⊕	M	+	+	+	?	..	..	..
170	+	+	⊕	—	..	..	..	..	..	..	..	..	..	..	..	..	..
171	⊕	+	+	..	..	..	..	..	..	..	..	..	..	..	..	..	..
172	—	⊕	+	+	S	+	..	..	..	..	..	..	..	..	..	..	..
173	⊕	M	M	M	+	+	M	..	..	..	..	..	..	..	..	..	..
174	M	S	S	⊕	M	..	..	..	..	..	..	..	..	..	..	..	..
175	M	S	S	⊕	M	..	..	..	..	..	..	..	..	..	..	..	..
176	+	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
177	M	⊕	S	M	..	..	..	..	..	..	..	..	..	..	..	..	..
178	M	M	M	M	—	⊕	+	+	+	+	+	+	+	..	..	..	..
179	+	⊕	—	—	—	+	+	+	+	+	—	+	..	..	..	..	..
180	+	—	⊕	+	+	+	+	+	+	—	+	..	..	..	..	..	..
181	M	+	+	+	⊕	—	+	+	..	..	..	..	..	..	..	..	..
182	+	+	⊕	—	+	..	..	..	..	..	..	..	..	..	..	..	..
183	+	⊕	+	+	—	..	..	..	..	..	..	..	..	..	..	..	..
184	⊕	+	+	+	..	..	..	..	..	..	..	..	..	..	..	..	..
185	—	—	—	⊕	—	+	+	+	..	..	..	..	..	..	..	..	..
186	+	+	+	M	M	⊕	⊕	..	..	..	..	..	..	..	..	..	..
187	⊕	+	+	..	..	..	..	..	..	..	..	..	..	..	..	..	..
188	S	S	+	—	+	—	—	+	+	—	⊕	S	S	..	..	..	..
189	⊕	—	+	+	—	+	+	..	..	..	..	..	..	..	..	..	..
190	S	S	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..
191	+	+	+	⊕	+	..	..	..	..	..	..	..	..	..	..	..	..
192	⊕	S	+	..	..	..	..	..	..	..	..	..	..	..	..	..	..
193	—	⊕	+	+	+	+	+	..	..	..	..	..	..	..	..	..	..
194	—	⊕	+	+	+	+	..	..	..	..	..	..	..	..	..	..	..
195	⊕	+	M	+	..	..	..	..	..	..	..	..	..	..	..	..	..
196	M	M	M	—	—	—	+	+	⊕	+	..	..	..	..	..	..	..
197	—	—	M	—	M	+	⊕	+	+	..	..	..	..	..	..	..	..
198	+	+	+	+	+	—	+	+	+	⊕	+	+	..	..	..	..	..
199	M	⊕	—	M	..	..	..	..	..	..	..	..	..	..	..	..	..
200	—	—	—	—	—	+	⊕	+	+	..	..	..	..	..	..	..	..
201	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
202	+	⊕	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..
203	⊕	—	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
204	+	⊕	+	..	..	..	..	..	..	..	..	..	..	..	..	..	..
205	+	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
206	—	⊕	+	+	+	..	..	..	..	..	..	..	..	..	..	..	..
207	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
208	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
209	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
210	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
211	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
212	M	S	S	S	⊕	+	..	..	..	..	..	..	..	..	..	..	..
213	+	⊕	+	..	..	..	..	..	..	..	..	..	..	..	..	..	..
214	⊕	+	+	..	..	..	..	..	..	..	..	..	..	..	..	..	..
215	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
216	+	+	+	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..
217	⊕	+	+	+	..	..	..	..	..	..	..	..	..	..	..	..	..
218	—	M	M	M	M	⊕	+	+	+	..	..	..	..	..	..	..	..
219	+	+	+	+	⊕	+	..	..	..	..	..	..	..	..	..	..	..
220	+	+	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..
221	M	M	M	⊕	+	..	..	..	..	..	..	..	..	..	..	..	..
222	M	M	M	⊕	+	+	+	+	..	..	..	..	..	..	..	..	..
223	M	⊕	+	+	+	+	+	..	..	..	..	..	..	..	..	..	..
224	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
225	—	⊕	+	+	..	+	..	..	..	..	..	..	..	..	..	..	..
226	+	+	+	+	⊕	—	—	—	..	..	..	..	..	..	..	..	..
227	M	+	⊕	+	+	+	+	..	..	..	..	..	..	..	..	..	..
228	S	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
229	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..

TABLE 10.—*Total Pregnancies in Five Hundred Families and Results as Tabulated—Continued*

Family Number	Number of Pregnancies																
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
230	+	+	⊕	M	..	..	..	..	..	..	..	..	..	..	..	..	..
231	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
232	+	⊕	+	M	..	..	..	..	..	..	..	..	..	..	..	..	..
233	⊕	+	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
234	—	—	+	⊕	—	M	M	..	..	..	..	..	..	..	..	..	..
235	⊕	M	—	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..
236	M	⊕	M	..	..	..	..	..	..	..	..	..	..	..	..	..	..
237	S	—	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..
238	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
239	⊕	+	M	M	..	..	..	..	..	..	..	..	..	..	..	..	..
240	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
241	M	+	M	⊕	+	..	..	..	..	..	..	..	..	..	..	..	..
242	⊕	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
243	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
244	—	⊕	+	..	..	..	..	..	..	..	..	..	..	..	..	..	..
245	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
246	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
247	+	⊕	+	+	M	M	..	..	..	..	..	..	..	..	..	..	..
248	M	S	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..
249	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
250	S	S	M	—	⊕	+	..	..	..	..	..	..	..	..	..	..	..
251	—	—	—	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..
252	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
253	M	—	—	⊕	+	+	+	+	..	..	..	..	..	..	..	..	..
254	+	+	+	+	⊕	M	M	M	..	..	..	..	..	..	..	..	..
255	+	+	⊕	—	—	—	M	..	..	..	..	..	..	..	..	..	..
256	⊕	+	—	..	..	..	..	..	..	..	..	..	..	..	..	..	..
257	+	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
258	—	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
259	⊕	S	—	M	+	..	..	..	..	..	..	..	..	..	..	..	..
260	+	+	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..
261	+	+	+	+	+	+	+	⊕	—	⊕	..	..	..	..	..	..	..
262	—	—	⊕	+	+	..	..	..	..	..	..	..	..	..	..	..	..
263	+	+	⊕	M	M	M	M	—	..	..	..	..	..	..	..	..	..
264	+	+	+	+	⊕	M	M	..	..	..	..	..	..	..	.	..	..
265	+	⊕	..	..	..	..	..	..	..	..	..	..	..	..	.	..	..
266	+	⊕	M	+	+	M	..	..	..	..	..	..	..	..	..	..	..
267	⊕	—	+	+	..	..	..	..	..	..	..	..	..	..	..	..	..
268	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
269	+	+	+	⊕	—	—	—	M	..	..	..	..	..	..	..	..	..
270	M	M	M	+	⊕	..	..	..	..	..	..	..	..	..	..	..	..
271	M	⊕	M	..	..	..	..	..	..	..	..	..	..	..	..	..	..
272	M	—	⊕	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..
273	+	+	+	⊕	—	M	..	..	..	..	..	..	..	..	..	..	..
274	⊕	—	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..
275	⊕	+	—	—	—	..	..	..	..	..	..	..	..	..	..	..	..
276	—	—	—	⊕	+	+	..	..	..	..	..	..	..	..	..	..	..
277	—	—	⊕	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..
278	⊕	M	+	+	..	..	..	..	..	..	..	..	..	..	..	..	..
279	—	—	M	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..
280	M	M	⊕	+	..	..	..	..	..	..	..	..	..	..	..	..	..
281	—	S	M	M	⊕	..	..	..	..	..	..	..	..	..	..	..	..
282	+	+	+	+	+	+	+	S	S	S	+	⊕	..	..	..	..	..
283	⊕	M	M	M	M	M	M	+	..	..	..	..	..	..	..	..	..
284	⊕	+	+	+	+	+	..	..	..	..	..	..	..	..	..	..	..
285	⊕	+	+	..	..	..	..	..	..	..	..	..	..	..	..	..	..
286	+	+	+	S	S	—	—	—	S	—	—	⊕	..	..	..	..	..
287	+	+	+	+	⊕	—	..	..	..	..	..	..	..	..	..	..	..
288	⊕	+	M	M	..	..	..	..	..	..	..	..	..	..	..	..	..
289	⊕	—	—	—	12 miscarriages				+	..	..	..	..	..	..	..	..
290	+	+	—	—	M	⊕	..	..	..	..	..	..	..	..	..	..	..
291	M	⊕	M	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..
292	—	⊕	+	+	M	..	..	..	..	..	..	..	..	..	..	..	..
293	⊕	—	+	+	..	..	..	..	..	..	..	..	..	..	..	..	..
294	⊕	+	+	+	..	..	..	..	..	..	..	..	..	..	..	..	..
295	—	—	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..
296	S	S	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..
297	—	⊕	—	—	M	..	..	..	..	..	..	..	..	..	..	..	..
298	+	—	+	+	+	+	⊕	..	..	..	..	..	..	..	..	..	..
299	+	+	S	+	+	⊕	..	..	..	..	..	..	..	..	..	..	..
300	—	+	+	⊕	+	+	..	..	..	..	..	..	..	..	..	..	..
301	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
302	+	⊕	—	+	+	..	..	..	..	..	..	..	..	..	..	..	..
303	⊕	⊕	—	+	+	..	..	..	..	..	..	..	..	..	..	..	..
304	+	+	+	+	+	+	+	+	+	⊕	..	..	..	..	..	..	..
305	+	+	—	—	+	⊕	..	..	..	..	..	..	..	..	..	..	..
306	—	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
307	S	⊕	+	M	..	..	..	..	..	..	..	..	..	..	..	..	..
308	—	⊕	+	—	S	M	M	..	..	..	..	..	..	..	..	..	..
309	⊕	—	+	..	..	..	..	..	..	..	..	..	..	..	..	..	..

TABLE 10.—*Total Pregnancies in Five Hundred Families and Results as Tabulated—Continued*

Family Number	Number of Pregnancies																
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
310	⊕	+	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
311	⊕	+	M	M	—	+	+	+	+	+	..	..	..	..	..	..	..
312	S	—	S	—	⊕	..	..	..	..	..	..	..	..	..	..	..	..
313	S	—	S	S	S	S	⊕	+	+	..	..	..	..	..	..	..	..
314	S	⊕	—	M	—	⊕	⊕	..	..	..	..	..	..	..	..	..	..
315	⊕	+	+	+	+	..	..	..	..	..	..	..	..	..	..	..	..
316	+	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
317	⊕	—	—	—	—	—	—	—	..	..	..	..	..	..	..	..	..
318	+	+	+	+	+	⊕	—	—	—	—	—	—	..	..	..	..	..
319	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
320	+	+	+	+	+	⊕	+	+	+	+	+	+	..	..	..	..	..
321	+	+	+	+	+	+	+	⊕	⊕	+	+	+	..	..	..	..	..
322	+	+	+	+	⊕	..	..	..	..	..	..	..	..	..	..	..	..
323	⊕	+	+	+	..	..	..	..	..	..	..	..	..	..	..	..	..
324	+	⊕	—	—	—	—	..	..	..	..	..	..	..	..	..	..	..
325	+	+	+	⊕	+	+	+	..	..	..	..	..	..	..	..	..	..
326	—	—	+	+	⊕	..	..	..	..	..	..	..	..	..	..	..	..
327	S	S	S	S	S	S	⊕	+	+	+	..	..	..	..	..	..	..
328	—	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
329	+	+	+	+	M	+	+	⊕	+	+	+	M	+	..	..	..	..
330	+	+	+	+	+	+	⊕	+	+	+	+	..	..	..	..	..	..
331	+	+	+	+	+	+	+	+	+	+	⊕	6 early deaths					
332	—	—	—	—	—	—	+	+	+	+	+	+	⊕	4+ children			
333	—	+	+	⊕	S	+	..	..	..	..	..	..	..	..	..	..	..
334	+	+	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..
335	+	+	⊕	+	+	..	..	..	..	..	..	..	..	..	..	..	..
336	⊕	+	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
337	+	+	+	⊕	M	M	..	..	..	..	..	..	..	..	..	..	..
338	+	+	+	+	+	⊕	+	+	..	..	..	..	..	..	..	..	..
339	M	+	+	+	..	..	..	..	..	..	..	..	..	..	..	..	..
340	⊕	+	—	+	+	+	+	M	+	M	+	..	..	..	..	..	..
341	S	S	⊕	—	..	..	..	..	..	..	..	..	..	..	..	..	..
342	+	+	⊕	—	+	+	—	..	..	..	..	..	..	..	..	..	..
343	⊕	—	—	+	+	M	M	..	..	..	..	..	..	..	..	..	..
344	+	+	⊕	+	..	..	..	..	..	..	..	..	..	..	..	..	..
345	—	M	M	⊕	+	+	..	..	..	..	..	..	..	..	..	..	..
346	+	+	+	⊕	+	—	+	..	..	..	..	..	..	..	..	..	..
347	M	S	⊕	+	—	—	..	..	..	..	..	..	..	..	..	..	..
348	—	⊕	M	..	..	..	..	..	..	..	..	..	..	..	..	..	..
349	+	⊕	+	+	+	..	..	..	..	..	..	..	..	..	..	..	..
350	⊕	—	M	—	+	M	—	M	M	+	+	M	+	..	..	..	..
351	S	S	M	S	M	S	⊕	+	..	..	..	..	..	..	..	..	..
352	+	⊕	+	+	+	..	..	..	..	..	..	..	..	..	..	..	..
353	+	+	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..
354	+	⊕	+	..	..	..	..	..	..	..	..	..	..	..	..	..	..
355	+	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
356	+	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
357	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
358	⊕	—	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
359	⊕	S	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
360	⊕	+	+	+	..	..	..	..	..	..	..	..	..	..	..	..	..
361	+	⊕	+	..	..	..	..	..	..	..	..	..	..	..	..	..	..
362	M	M	M	M	+	⊕	+	+	+	+	+	+	+	..	..	..	..
363	+	—	⊕	—	+	+	+	+	+	—	+	..	..	..	..	..	..
364	+	—	—	—	⊕	+	+	+	+	+	—	..	..	..	..	..	..
365	M	+	+	+	⊕	—	+	+	..	..	..	..	..	..	..	..	..
366	+	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
367	+	+	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..
368	M	⊕	S	M	..	..	..	..	..	..	..	..	..	..	..	..	..
369	+	+	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..
370	⊕	+	+	+	+	+	..	..	..	..	..	..	..	..	..	..	..
371	+	+	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..
372	M	M	S	⊕	+	..	..	..	..	..	..	..	..	..	..	..	..
373	+	+	—	+	+	+	⊕	+	—	+	—	+	..	..	..	..	..
374	+	+	+	⊕	+	+	+	+	..	..	..	..	..	..	..	..	..
375	+	+	⊕	—	—	..	..	..	..	..	..	..	..	..	..	..	..
376	+	+	—	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..
377	+	M	⊕	M	M	⊕	+	—	..	..	..	..	..	..	..	..	..
378	—	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
379	S	—	—	—	⊕	+	+	+	+	+	+	..	..	..	..	..	..
380	+	+	⊕	—	..	..	..	..	..	..	..	..	..	..	..	..	..
381	⊕	+	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
382	M	M	—	⊕	+	+	+	..	..	..	..	..	..	..	..	..	..
383	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
384	M	⊕	M	+	+	..	..	..	..	..	..	..	..	..	..	..	..
385	—	M	⊕	+	+	+	..	..	..	..	..	..	..	..	..	..	..
386	M	M	—	—	⊕	⊕	+	..	..	..	..	..	..	..	..	..	..
387	—	—	⊕	+	+	+	..	..	..	..	..	..	..	..	..	..	..
388	—	—	⊕	+	+	+	..	..	..	..	..	..	..	..	..	..	..

TABLE 10.—*Total Pregnancies in Five Hundred Families and Results as Tabulated—Continued*

Family Number	Number of Pregnancies															
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
389	⊕	—	—	+	+	+	+	+	..	..	..	..	..	..	..	..	..
390	—	⊕	+	+	+	+	+	+	..	..	..	..	..	..	..	..	..
391	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
392	—	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
393	⊕	+	+	..	..	..	..	..	..	..	..	..	..	..	..	..	..
394	M	M	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..
395	+	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
396	+	—	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..
397	+	+	+	+	+	+	⊕	..	..	..	..	..	..	..	..	..	..
398	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
399	—	—	—	⊕	+	..	..	..	..	..	..	..	..	..	..	..	..
400	S	S	+	+	—	⊕	..	..	..	..	..	..	..	..	..	..	..
401	M	—	M	M	S	M	⊕	+	+	..	..	..	..	..	..	..	..
402	⊕	M	S	..	..	..	..	..	..	..	..	..	..	..	..	..	..
403	M	—	—	⊕	+	+	..	..	..	..	..	..	..	..	..	..	..
404	—	⊕	—	..	..	..	..	..	..	..	..	..	..	..	..	..	..
405	M	M	M	⊕	+	+	+	..	..	..	..	..	..	..	..	..	..
406	—	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
407	M	M	+	S	⊕	M	..	..	..	M	..	..	..	..	..	..	..
408	—	—	—	—	—	⊕	+	⊕	—	M	⊕	..	..	..	..	..	..
409	M	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
410	—	M	—	—	⊕	M	M	M	M	S	..	..	..	..	..	..	..
411	+	M	M	⊕	—	+	+	..	..	..	..	..	..	..	..	..	..
412	S	⊕	+	+	..	..	..	..	..	..	..	..	..	..	..	..	..
413	M	S	—	M	⊕	..	..	..	..	..	..	..	..	..	..	..	..
414	M	—	⊕	+	..	..	..	..	..	..	..	..	..	..	..	..	..
415	M	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
416	+	⊕	M	..	..	..	..	..	..	..	..	..	..	..	..	..	..
417	M	M	M	S	S	—	—	—	+	—	M	—	M	M	⊕	—	+
418	M	M	M	S	M	⊕	..	..	..	..	..	..	..	..	..	..	..
419	M	—	—	—	⊕	+	+	+	+	..	..	..	..	..	..	..	..
420	—	—	—	—	—	—	—	⊕	—	—	..	..	..	..	..	..	..
421	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
422	+	+	+	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..
423	M	—	M	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..
424	+	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
425	+	+	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..
426	M	M	M	—	⊕	..	..	..	..	..	..	..	..	..	..	..	..
427	M	—	—	—	⊕	+	+	+	+	+	+	..	..	..	..	..	..
428	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
429	⊕	—	+	..	..	..	..	..	..	..	..	..	..	..	..	..	..
430	M	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
431	+	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
432	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
433	—	⊕	+	+	+	..	..	..	..	..	..	..	..	..	..	..	..
434	—	—	—	⊕	+	..	..	..	..	..	..	..	..	..	..	..	..
435	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
436	M	..	—	+	+	⊕	..	..	..	..	..	..	..	..	..	..	..
437	+	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
438	M	⊕	M	+	..	..	..	..	..	..	..	..	..	..	..	..	..
439	—	⊕	+	—	M	M	M	—	+	..	..	..	..	..	..	..	..
440	⊕	—	+	+	+	+	..	..	..	..	..	..	..	..	..	..	..
441	M	—	⊕	—	M	+	..	..	..	..	..	..	..	..	..	..	..
442	—	+	+	+	+	⊕	—	+	+	..	..	..	..	..	..	..	..
443	S	⊕	+	..	..	..	..	..	..	..	..	..	..	..	..	..	..
444	+	⊕	+	—	..	..	..	..	..	..	..	..	..	..	..	..	..
445	+	+	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..
446	M	M	—	—	+	⊕	..	..	..	..	..	..	..	..	..	..	..
447	+	+	M	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..
448	M	M	M	M	M	M	M	M	M	⊕	+	..	..	..	..	..	..
449	⊕	+	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
450	⊕	+	M	+	M	+	..	..	..	..	..	..	..	..	..	..	..
451	—	—	⊕	+	..	..	..	..	..	..	..	..	..	..	..	..	..
452	S	—	M	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..
453	M	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
454	+	⊕	+	+	—	..	..	..	..	..	..	..	..	..	..	..	..
455	—	—	M	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..
456	S	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
457	S	⊕	+	M	..	..	..	..	..	..	..	..	..	..	..	..	..
458	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
459	—	S	⊕	M	+	+	+	+	..	..	..	..	..	..	..	..	..
460	M	—	+	⊕	+	+	..	..	..	..	..	..	..	..	..	..	..
461	+	+	+	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..
462	+	⊕	+	—	+	+	..	..	..	..	..	..	..	..	..	..	..
463	+	+	—	—	⊕	+	..	..	..	..	..	..	..	..	..	..	..
464	+	M	M	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..
465	+	⊕	—	—	M	..	..	..	..	..	..	..	..	..	..	..	..
466	M	⊕	+	M	M	+	M	+	..	..	..	..	..	..	..	..	..
467	+	+	—	—	—	⊕	+	..	..	..	..	..	..	..	..	..	..

TABLE 10.—*Total Pregnancies in Five Hundred Families and Results as Tabulated—Continued*

Family Number	Number of Pregnancies																
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
468	—	+	+	—	+	+	+	⊕	+	+	..	..	..	..	..	..	..
469	⊕	+	M	..	..	..	..	..	..	..	..	..	..	..	..	..	..
470	+	+	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..
471	⊕	+	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
472	—	+	⊕	+	..	..	..	..	..	..	..	..	..	..	..	..	..
473	+	+	⊕	—	—	..	..	..	..	..	..	..	..	..	..	..	..
474	—	—	—	⊕	—	—	+	..	..	..	..	..	..	..	..	..	..
475	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
476	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
477	M	M	S	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..
478	⊕	+	S	..	..	..	..	..	..	..	..	..	..	..	..	..	..
479	M	M	⊕	+	..	..	..	..	..	..	..	..	..	..	..	..	..
480	M	⊕	+	+	—	—	..	..	..	..	..	..	..	..	..	..	..
481	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
482	S	⊕	M	..	..	..	..	..	..	..	..	..	..	..	..	..	..
483	—	M	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..
484	—	—	—	—	—	—	—	—	⊕	..	..	..	..	..	..	..	..
485	+	+	⊕	+	+	..	..	..	..	..	..	..	..	..	..	..	..
486	+	M	⊕	—	..	..	..	..	..	..	..	..	..	..	..	..	..
487	S	⊕	M	..	..	..	..	..	..	..	..	..	..	..	..	..	..
488	+	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
489	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
490	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
491	⊕	S	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
492	S	+	—	—	—	⊕	+	..	..	..	..	..	..	..	..	..	..
493	+	+	+	+	+	M	⊕	M	M	+	M	+	M	M	+	—	..
494	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
495	M	S	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..
496	+	M	+	—	—	—	⊕	+	—	+	M	M	M	..	..	..	..
497	+	+	+	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..
498	—	—	—	⊕	+	..	..	..	..	..	..	..	..	..	..	..	..
499	+	+	+	+	+	⊕	+	+	..	..	..	..	..	..	..	..	..
500	+	+	+	⊕	+	..	..	..	..	..	..	..	..	..	..	..	..

DISCUSSION

DR. JOHN H. STOKES, Philadelphia: This paper, which is very clearly a large and thoroughly digested experience should, I think, have an early publication. There is one point on which I venture to disagree, and that is the rating of lack of funds as a minor consideration. I think this is all too frequently a major consideration in all aspects of medicine. The work that has heretofore been done in heredosyphilis has been very sketchy. There has not been a successor of Hutchinson and of Fournier, unless one is now to rate Dr. Smith in that capacity. Certainly, a thorough review of 1,000 cases is a monumental achievement.

To me the most interesting point of Dr. Smith's presentation was the demonstration of the value of treatment. I would like to raise the question as to his experience in the prevention of interstitial keratitis by treatment of the child before the onset of the complication. The report of Carvill and Derby in the *Boston Medical and Surgical Journal* should be broadcast over the medical world. These authors, while demonstrating conclusively the immense value of modern treatment in dealing with interstitial keratitis, felt obliged to take a pessimistic view of preventive possibilities. The question of the alteration of osseous stigmas by antenatal treatment is also one of much interest, and one thus far very little studied. For example, a patient under my observation who was treated for syphilis from within six weeks of birth and gave negative reactions serologically, and apparently was well in her fifth year, none the less had Hutchinsonian teeth of the upper jaw which were demonstrable by the roentgen ray. The lack of an experimental background for the investigation of

heredosyphilis throws the burden of progress back on the clinician and he should rise to his responsibilities in this field. Dr. Smith's presentation is an opening gun of high caliber.

Dr. Harold N. Cole, Cleveland: Statistics are difficult to follow, but I agree with Dr. Stokes that this is a piece of work which can be studied and much benefit gained therefrom. In the treatment of interstitial keratitis in which there is not a satisfactory reaction to potassium iodide and other treatments, I have obtained a rapid response to 5 cc. of boiled milk every three to five days. This foreign protein has been helpful in these cases.

Dr. Richard L. Sutton, Kansas City, Mo.: Dr. Cole has brought up a point which I consider important. About four years ago, acting on a suggestion of Dr. W. W. Duke's, I began the use of foreign protein injections in certain resistant cases of syphilis. Instead of milk, I employed typhoid bacterin, or colon vaccine. Patients who have not responded favorably to ordinary and even intensive methods of treatment, often improve rapidly following a few doses of such a foreign protein. I heartily approve Dr. Cole's suggestion.

Dr. John E. Lane, New Haven, Conn.: I was much interested in the case of bilateral synovitis of the knee which Dr. Smith reported. These cases are almost always overlooked unless the opthalmologists happen to see them.

There is one question I would like to ask: In Dr. Smith's series of cases of keratitis have there been any cases of scleritis? I have recently had several of those, and it is even more difficult to get prompt results from treatment than in interstitial keratitis.

Dr. William H. Guy, Pittsburgh: The question of prevention, as pointed out by Dr. Smith, is of the utmost importance and my experience may be of significance. In the University Maternity Hospital all patients with a positive Wassermann reaction are referred for specific medication, a Wassermann test being made on every patient admitted, and there being about 1,800 deliveries yearly. Treatment is given in courses up to the time of delivery and is begun again as soon as possible afterward. Infants are examined immediately after birth. In the four years I have been doing this work I have seen only two cases of interstitial keratitis, and clinical examples of congenital syphilis have been exceedingly rare. I realize, of course, that the late appearance of keratitis and the difficulty of keeping track of children probably accounts to some extent for my low figures. In a study of 160 cases of interstitial keratitis from the University of Pittsburgh Free Dispensary my observations were in agreement with most of the points made by the essayist. The histologic nature of interstitial keratitis is essentially that of gumma and, while opinions are at variance, the consensus seems to be that it is an active syphilid. Spirochetes have been demonstrated repeatedly in experimental keratitis, and Von Hippel found them in a keratitis occurring in a 33 week old fetus. Dr. Wile has seen spirochetes in active cases. Due to the character of the lesion histologically one naturally concludes that iodides should play a prominent part in the treatment of interstitial keratitis. Evaluation of results of determination of final vision is unfair in its frequent suggestion of therapeutic inadequacy, because all cases leave scars, as originally demonstrated with the slit lamp by Koegge; further the position of scars materially varies final vision—a scar at the periphery will interfere but little; at the center of the cornea the same scar may materially impair vision. The urgency of early and long continued treatment, not only to clear the eye and to prevent recurrence, but also directed toward ultimate cure of the patient, has been well emphasized by Dr. Smith.

Bearing on the question of etiology, I would call attention to the work of Pearce and Brown, in which they were able to increase or decrease the incidence of keratitis in experimental rabbit syphilis by varying local and general tissue reactions. They conclude that the tendency to relapse in keratitis, as well as the peculiar circumstances of its occurrence, is probably to be explained by the degree of protection afforded the eyes by reactions elsewhere, and the feeble protection developed by reactions in these tissues.

Dr. Kendal P. Frost, Los Angeles: In Los Angeles I have had a small clinic for children at the hospital which has recently been interrupted by an epidemic of infantile paralysis, during which time the clinic was closed and I did not obtain figures. However, some observations have been made, particularly by Dr. Linthicum, who has been testing these patients out on changes in the vestibular apparatus of the eighth nerve, and has found a high incidence of disturbance in its mechanism. Routine cerebrospinal fluid examinations have also been made with very few positive reactions. In the cases in which they were positive practically the only thing that was abnormal was the positiveness of the Wassermann reaction. The cells were not increased, and the globulin was not positive.

Dr. Jay Frank Schamberg, Philadelphia: Dr. Smith has presented to us an excellent summary of congenital syphilis based on a large experience. I have always been much interested in the asymptomatic cases in which nothing is evident save a positive Wassermann reaction. There will be found, at times, in the families of syphilitic patients, four, five or six children with positive Wassermann reactions, but without stigmas of syphilis—Hutchinson teeth, cutaneous eruptions, deafness, etc., may all be absent. In many of these cases there is a "constitutional inferiority," manifested by anemia and subnormal weight, but in some even these symptoms are absent. An interesting query is "what is the ultimate fate of these patients? What will the actuary tables show as to the longevity of these children?" It would be valuable for this association to make a statistical study of the ultimate history of children of syphilitic parentage. My associate, Dr. Wright, has in my clinic recently studied the comparative effects of various antisyphilitic remedies on the Wassermann reaction in congenital syphilis. He has found that bismuth is more potent in reversing a positive Wassermann reaction than the other drugs; this is particularly true after a course of neoarsphenamine. In one large group, 50 per cent of the cases showed a reversal of the Wassermann reaction after thorough treatment with bismuth.

Dr. Samuel E. Sweitzer, Minneapolis: I think the most important consideration in hereditary syphilis is the prevention. Evidently, the treatment of the pregnant woman is still neglected. The most important way to prevent the appearance of syphilitic children is to treat the pregnant syphilitic mother, and to give intensive early treatment. The earlier and more intensive the treatment the less the number of syphilitic children. There are still thousands and thousands of these children, so there must be some slowing up in the treatment somewhere.

Dr. Harry E. Alderson, San Francisco: I should like to ask how far one can go in the treatment of pregnant syphilitic women. At Stanford University there are many pregnant syphilitic patients. The social service department is active and it succeeds in rounding up numerous families of syphilitic patients, so syphilitic women are often seen early in their pregnancy. I am in the habit of treating them energetically, sometimes possibly exceeding the point of safety.

There have been no accidents, but still I have wondered whether too many chances are being taken in giving this intensive treatment in pregnancy. I treat the patients just as intensively and energetically as other patients in good physical condition. They are given just as much arsphenamine, mercury and bismuth as I dare give. I should like to know how far one may go with these cases.

DR. C. GUY LANE, Boston: The remarks of Dr. Alderson recalled a case in the list Dr. Smith mentioned, in which a fatality occurred immediately after an arsphenamine injection in one of the pregnant patients. That raised in my mind the question Dr. Alderson mentioned as to pushing the treatment in these cases.

I also wish to emphasize the value of follow-up and the social work in these cases. The Massachusetts General Hospital, as Dr. Smith stated, is separated by about two miles from the maternity hospital. The women go there to the prenatal clinic and blood is taken for the Wassermann test, and they are then referred to the other clinic. Some of them get there, some do not, and some get there late. When they come for treatment they are referred back to the Lying-in Hospital, or to the station nearest their residence for observation. Between the two clinics an attempt is made to follow the patients up to the point of delivery. Then they return to the Lying-in Hospital. Then to refer them to the other department for further treatment and follow-up is another jump. Some will return in two or three weeks, some not until later, and some do not come back at all. The follow-up and the cooperation of the social service work of the two departments, I think, is just as essential in the therapy as the use of arsphenamine or bismuth.

DR. HENRY H. HAZEN, Washington, D. C.: I would like to know what are Dr. Smith's criteria for freedom from congenital syphilis in children born under suspicious circumstances.

DR. C. MORTON SMITH, Boston: In regard to Dr. Stoke's remark concerning finances, the statement was made with a question mark. It is not always easy for the social worker to raise the necessary funds.

It was impossible to cover, in the time allotted me, all the points that will appear in the published article. There is no uniformity of opinion among ophthalmologists regarding the value of arsphenamine treatment of interstitial keratitis, although I believe the majority are convinced of the benefits of such treatment.

I agree with Dr. Guy that some of the cases show only a small opacity, and increasing the potassium iodide has as good effect in these as on lesions in other parts of the body. The iodide is certainly of value in clearing up the products of inflammation. Interstitial keratitis has been regarded as a direct spirochetal infection. Cases have been reported in which spirochetes were found in the corneal lesion. There has been a small number of optic atrophies and choroidal changes in the cases reported.

The paper deals with the necessity of following up the children in syphilitic families when they may not show any clinical evidences of the disease for a long time. They must be kept under observation and treated when necessary.

I have not seen any reason for not giving intensive treatment in cases of pregnancy, and the earlier it can be given the better the result. If arsphenamine is given early in pregnancy, it may be possible to modify even the dental defects which have their origin in about the third or fourth month of intrauterine life. The sudden fatality that Dr. Guy Lane referred to, following intravenous arsphenamine was due to the use of a solution erroneously sent me

as physiologic sodium chloride solution, and so labelled, and the mistake was not detected until after the injection had been given; so his remarks are not an argument against a proper preparation of arsphenamine being used in pregnancy. I have usually increased the number and given slightly subnormal doses in pregnancy.

In answer to Dr. Lane's question: There have been a few cases of scleritis, not enough to make any particular impression on us one way or the other. I think the cases that have been followed closely were thrown out as being of nonspecific origin.

As to Dr. Hazen's question regarding criteria, I think when there is a definite history of syphilis, or even a history of alcoholism in either parent, it is strong presumptive evidence of syphilis in the child. It seems to me that these children should be given the benefit of the doubt, and kept under observation as long as possible. I have some patients that I have followed for years, and they now have children of their own. This shows the value of long continous service.

DR. HAZEN: I have found syphilitic changes in the umbilical cord, and yet the child did not show evidence of syphilis and gave a negative Wassermann reaction, for some time. Would you regard that child as having syphilis or not?

DR. SMITH: Yes, a potential syphilis—if the mother has syphilis the child has syphilis.

BISMUTH THIOGLYCOLLATE IN EXPERIMENTAL AND CLINICAL TREATMENT OF SYPHILIS*

O. M. GRUHZIT, M.D., EDWARD LYONS, PH.D.

AND

RALPH PERKINS, M.D.

DETROIT

With the advent of bismuth therapy in syphilis it has become evident that the insoluble and soluble bismuth preparations suspended in organic oils are absorbed slowly,[1] because they are insoluble to begin with, or are rendered insoluble because of the unstable chemical nature.[2]

Besides having a slow rate of absorption, some of the present bismuth preparations produce lumps and cause pain, and occasionally death may result from oil embolism after an accidental injection into the blood stream.[3]

The present water soluble bismuth preparations either are too toxic or produce too severe an injury at the site of injection to be of practical value in the treatment of syphilis.[4]

With this in view it was necessary to search for a bismuth preparation which would be free from the foregoing undesirable features.

In a series of soluble bismuth compounds prepared by one of us (Lyons), a bismuth derivative of thioglycollic acid was the most satisfactory compound so far found. It is soluble in water; has relatively low toxicity; causes neither pain nor tissue destruction at the site of injec-

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* From the Research Laboratories of Parke, Davis and Company, and the Detroit Dermatologic Clinic.

1. Cole, N. H.; Farmer, H. L., and Miskdjian, H.: The Intramuscular Absorption of Some Insoluble Bismuth Compounds as Revealed by the Roentgen-Ray, Arch. Dermat. & Syph. **13**:219 (Feb.) 1926. Beinhauser, L. G., and Jacob, F. M.: The Relative Absorption and Therapeutic Efficiency of Some Bismuth Preparations, Am. J. Syph. **9**:213, 1925. Parnell, R. J. G.: Bismuth in Treatment of Syphilis, Proc. Roy. Soc. Med. **17**:19, 1926. Gruhzit, O. M.: Bismuth Salicylate in Experimental Rabbit Syphilis, Arch. Dermat. & Syph. **13**:195 (Feb.) 1926.

2. Corfield, B. C. E., and Adams, F. W.: Bismuth and Sodium Bismuth Tartrates, Pharm. J. **57**:80, 1923. Gruhzit (footnote 1, fourth reference).

3. Sutton, I. C.: The Bismuth Treatment of Syphilis, Am. J. Syph. **9**:600, 1925. Wolf, Max: Ueber Lokale embolische Bismutschädigungen, Wien. klin. Wchnschr. **38**:1160, 1925. Cole, Parnell and Gruhzit (footnote 1, first, third and fourth references).

4. Levaditi, C.: Le bismuth dans le traitement de la syphilis, Paris, Masson et Cie., 1924. Klauder, J. V.: Bismuth in the Treatment of Syphilis, Arch. Dermat. & Syph. **7**:721 (June) 1923.

tion; has no cumulative action, and has a spirocheticidal effect in therapeutic doses. This compound, therefore, was selected and studied as to its adaptability in the treatment of syphilis.

Physical Nature.—This compound is the trisodium salt of bismuth thioglycollic acid and is for convenience referred to as bismuth thioglycollate.

Its structural formula is as follows:

$$\begin{array}{r} SCH_2COONa \\ Bi-SCH_2COONa \\ SCH_2COONa \end{array}$$

It is a light yellowish amorphous powder, contains 38.02 per cent of metallic bismuth and possesses a slight odor of garlic. In powder form it is stable, but in solution it undergoes decomposition on standing. It is freely soluble in water and is slightly alkaline in reaction. It neither precipitates serum nor possesses corrosive action to tissues. The solution is clear, slightly yellowish and stable for a short period of boiling, but it is decomposed on prolonged boiling.

Toxicity.—The chronic toxicity to animals varies slightly between different animals. The minimum lethal dose intraperitoneally for guinea-pigs and rats fluctuates between from 10 to 12 mg. of metallic bismuth per kilogram of body weight. The tolerating dose for the foregoing animals ranges between 8 and 10 mg. of metallic bismuth per kilogram of body weight. For rabbits the minimum lethal dose and the tolerating dose given intramuscularly are about the same as for guinea-pigs and rats. Intravenously, the minimum lethal dose for rabbits is from 8 to 10 mg., and the tolerating dose from 6 to 8 mg., of metallic bismuth per kilogram of body weight; i. e., it is only slightly more toxic intravenously than intramuscularly. On an average the tolerated dose intramuscularly is about 24 mg. of the substance, and intravenously it is about 18 mg. per kilogram of body weight.

Albuminuria.—Six apparently healthy rabbits were treated in pairs with 0.25, 0.50 and 1.0 mg. of bismuth per kilogram of body weight. The urine was examined frequently for the presence of albumin. After the first injection, faint traces of albumin appeared in the urine of rabbits treated with 1.0 mg. of bismuth per kilogram, but not in that of rabbits treated with 0.25 or 0.50 mg. per kilogram. On the third day one of each pair of rabbits was killed for the study of histologic changes in the organs. The remaining three rabbits were treated eight times each. After the second injection the trace of albumin disappeared entirely in the rabbit receiving 1.0 mg. per kilogram of body weight. For the rabbit which received 0.25 mg. per kilogram at the beginning, the dose was increased after the third treatment to 0.50 mg. per kilogram; this dosage was repeated twice, after which it was increased to 0.75 mg. per

kilogram. Albuminuria did not appear in this or other rabbits treated with 0.75 mg. of bismuth per kilogram of body weight. In addition to the rabbits mentioned, two normal dogs received a course of ten injections of 0.5 and 0.75 mg. of bismuth per kilogram in periods of from two to four days. The dogs did not show albuminuria during a period of forty-five days. Syphilitic rabbits which received a dose of from 0.5 to 0.75 mg. of bismuth in a course of treatment did not show albumin in the urine. Larger doses administered to syphilitic rabbits (1.0 mg per kilogram) would occasionally show traces of albumin in the urine.

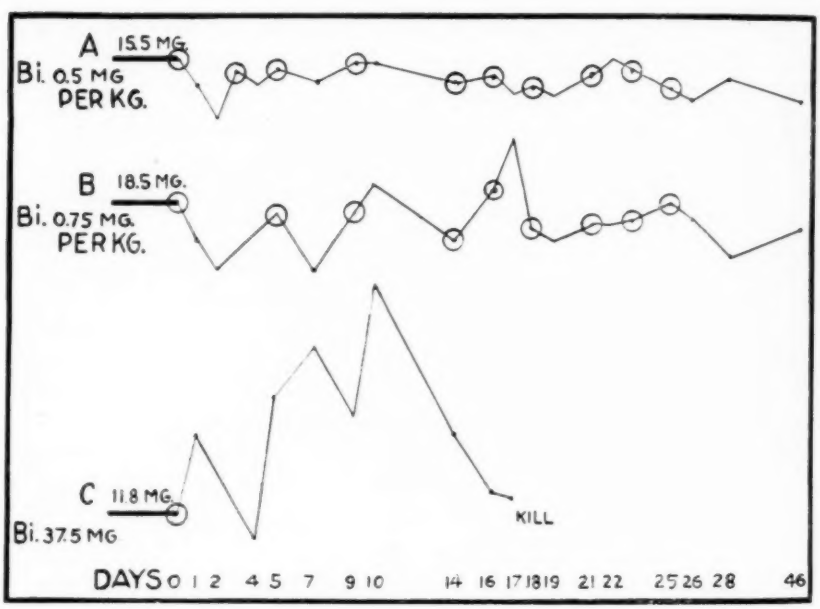

Fig. 1.—Blood urea nitrogen changes under bismuth thioglycollate treatment. Dog *A* received a course of 0.5, dog *B*, 0.75, and dog *C*, a single injection of 2.8 mg. of bismuth per kilogram of body weight.

Blood Urea Nitrogen Retention.—To elucidate further the effect of bismuth thioglycollate on the kidneys, the blood urea nitrogen was determined before and after the treatment. The dogs were bled four times during a preliminary study of a normal condition; the average of the four determinations is presented as a heavy line in figure 1. Dogs *A* and *B* received a cumulative treatment of 0.5 and 0.75 mg. of bismuth per kilogram of body weight, respectively. Dog *C*, weighing 13.4 Kg., received one human dose of 37.5 mg. of bismuth, or 2.8 mg. of bismuth per kilogram, which is from 3.7 to 5.6 times more than a therapeutic dose.

The samples of blood were taken in the morning before feeding and before treatment. The bleeding was repeated twenty-four, forty-eight,

seventy-two hours, etc., after treatment. Dogs *A* and *B* each received ten injections. In the beginning, the intervals between the injections were longer, so that the effect of a single dose could be noted; the last six injections were bunched together in order that the response to an intensive treatment might be observed.

The curves *A* and *B* of the dogs receiving 0.5 and 0.75 mg. of bismuth per kilogram, respectively, show no deviation from the normal to consider the possibilities of kidney injury. Examinations of the urine of these dogs did not at any time show the presence of albumin. It prob-

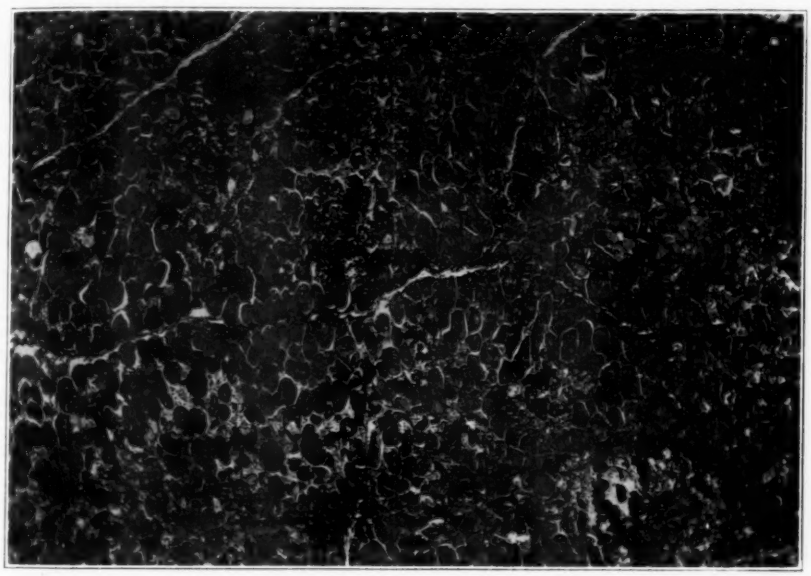

Fig. 2.—Bismuth thioglycollate, 0.1 Gm., in muscle; excised in forty-eight hours; slight degree of Zenker's necrosis, some edema, occasionally small hemorrhage.

ably can be considered that neither 0.5 nor 0.75 mg. of bismuth per kilogram had injurious effects on the kidneys.

The curve *C* presents the blood urea nitrogen after a single injection of 2.8 mg. of bismuth per kilogram of body weight. Considerable retention of blood urea nitrogen was noted from the fifth to the fourteenth day after the treatment, but the injury to the kidneys must have been only transitory as the last three blood urea determinations are within the limits of normal fluctuations, and albumin did not appear in the urine during the height of urea retention.

Microscopic Changes in Various Organs.—Lethal doses in rabbits produced severe necrosis in all organs. An acute or prolonged injury of the cells was rarely accompanied by calcium deposits. Histologic studies

of the tissues of animals killed seventy-two hours after treatment with from 1.0 to 4.0 mg. of bismuth per kilogram indicate that the dose of 1 mg. of bismuth per kilogram did not produce changes in the liver, spleen or pancreas, which could be distinguished from a normal condition. The kidneys showed some congestion and cloudy swelling, and in some cases, focal calcium deposits were present in the area between the cortex and the medulla. The straight tubules contained some hyaline casts. Desquamation or fatty degeneration of the epithelium of the tubules was not noted.

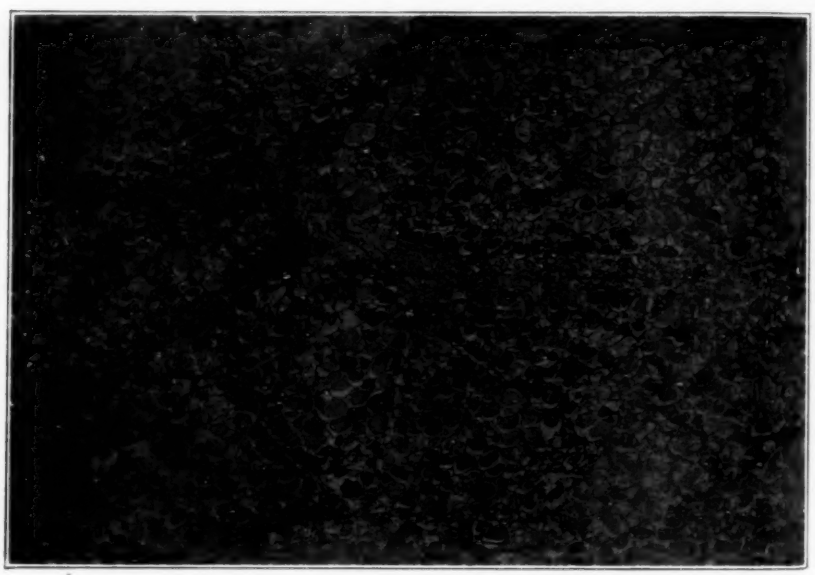

Fig. 3.—Bismuth potassium tartrate injected intramuscularly in water, 0.09 Gm.; excised in forty-eight hours; tissues entirely necrotic; bismuth precipitated into an insoluble form.

A dose of 2 mg. of bismuth per kilogram showed considerable necrosis in all organs. A dose of 4 mg. of bismuth per kilogram produced a rather severe injury to all organs which differed only in degree from that produced by 2 mg. of bismuth per kilogram.

The therapeutic dose of from 0.5 to 0.75 mg. of bismuth or from 1.3 to 2 mg. of the salt per kilogram of body weight, administered to rabbits in a single dose or in a cumulative course of ten injections, did not produce any histologic changes in the organs which could not also be found in normal rabbits. In some rabbits, however, a dose of from 0.75 to 1 mg. of bismuth per kilogram of body weight, at the end of a course of treatment of from seven to ten injections, indicated the presence of

some cloudy swelling in the liver cells and in the tubuli contorti epithelium.

Absorption.—When injected intramuscularly the substance was almost immediately absorbed and distributed throughout the body. Animals injected with 0.1 Gm. into the lumbar muscles and killed, some immediately after the injection and others at intervals of from one to two hours, did not show bismuth at the site of injection after two hours,

TABLE 1.—*Number and Time of Treatments with Bismuth Thioglycollate*

Rabbit	Metallic Bismuth, Mg. per Kg.	Days of Treatment										Number of Treatments	Time of Lymph Node Transplant
		1	2	3	4	5	6	7	8	9	10		
319	0.25	0	2	5	8	9	11	14	17	..	.	8	..
317	0.25	0	2	5	8	11	14	17	..	..	..	7	..
316	0.25	0	2	5	8	11	14	17	..	..	..	7	..
319a	0.50	0	2	5	..	..	..	..	..	..	..	3	7
317a	0.50	0	2	5	9	14	17	21	26	..	..	8	29
316a	0.50	0	2	5	9	14	17	21	26	..	..	8	29
312	0.50	0	2	5	8	11	14	17	21	23	26	10	35
351	0.50	0	2	5	8	11	14	17	21	23	26	10	39, 126
361	0.50	0	2	5	8	11	14	17	21	23	26	10	39, 126
275	0.50	0	2	4	6	8	12	19	21	29	32	10	52
300	0.50	0	2	5	10	24	28	30	37	41	44	10	15, 67
315	0.50	0	2	5	9	11	15	18	..	..	..	7	19
357	0.50	0	2	5	9	11	14	17	22	26	..	9	29
183	0.50	0	2	3	5	8	11	14	17	20	..	9	31
447	0.60	0	2	4	7	11	14	17	22	24	28	10	39
446	0.60	0	2	4	7	11	14	17	22	24	28	10	44
438	0.60	0	2	4	7	11	14	17	22	24	28	10	44
397	0.60	0	2	4	7	11	14	17	22	24	28	10	44
364	0.75	0	2	4	8	11	14	17	21	23	26	10	50
369	0.75	0	2	4	8	11	14	17	21	23	26	10	39, 67
318	0.75	0	3	6	7	11	15	..	..	..	..	6	20
314	0.75	0	2	5	9	11	15	18	21	26	..	9	18, 50
397a	0.75	0	3	6	10	14	19	21	26	..	..	8	30
438a	0.75	0	3	6	10	14	19	21	26	..	..	8	28
446a	0.75	0	3	6	10	14	19	21	..	..	..	7	27
429	0.75	0	3	7	11	16	20	31	..	..	..	7	26
316b	0.75	0	3	7	11	16	20	31	..	..	..	6	32
700	0.77	0	2	5	8	11	14	17	19	22	..	9	53
313	1.0	0	2	5	7	11	14	18	22	..	..	8	35
321	1.0	0	2	5	7	11	14	18	22	..	..	8	35
198	1.0	0	2	5	4	12	19	23	27	..	..	8	37
449	1.0	0	2	7	11	16	20	31	..	..	..	7	26
361b	1.0	0	2	7	11	16	20	31	..	..	..	7	26
96	2.0	0	2	4	..	..	..	..	..	..	..	3	23
463	2.0	0	..	..	..	..	..	..	..	..	..	1	38
445	3.0	0	..	..	..	..	..	..	..	..	..	1	..
481	4.0	0	..	..	..	..	..	..	..	..	..	1	..
489	5.0	0	..	..	..	..	..	..	..	..	..	1	..
436	6.0	0	..	..	..	..	..	..	..	..	..	1	..

when the excised site was placed either in hydrogen sulphide solution or in a yellow sulphide of ammonia. Histomicrochemical study also failed to reveal bismuth in the two hour specimen, but occasionally some bismuth would be observed in the one hour period specimen.

Site of Injection.—Injections of soluble salts of mercury, bismuth and arsenic, intramuscularly, cause severe necrosis of the tissues at the injected site; bismuth thioglycollate, on the contrary, causes only slight injury in the form of Zenker's necrosis and a slight degree of fatty degeneration of the muscle cells, and edema.

The relatively slight injury from bismuth thioglycollate at the site of injection shows that the compound is not corrosive to tissue cells, and

that it does not form albuminate compounds of bismuth, as compared with the considerable destruction and necrosis produced by potassium bismuth tartrate.

Spirocheticidal Study.—For the study of the effect on spirochetes the Major Nichol's strain of *Spirochaeta pallida* was used as it is probably the most virulent type in the hands of laboratory workers. The inoculation was done in one or both testes of rabbits. When marked

TABLE 2.—*Spirocheticidal Effect of Bismuth Thioglycollate*

Rabbit	Metallic Bismuth, Mg. per Kg.	Bismuth Thioglycollate, Mg. per Kg.	Days Treated and Dark-Field Results*													
			0+	1	2+	3	4	5+	7	9+	10	11+	14+	17+	21+	23+
319	0.25	0.67	4x	..	x	4x	4x	4x	4x	x	9+	4x	4x	4x	4x	4x
317	0.25	0.67	4x	..	4x	—	—	x	—	—	—	—	—	4x	4x	4x
316	0.25	0.67	4x	..	4x	4x	4x	4x	—	—	—	4x	4x	4x	4x	4x
319a	0.50	1.3	4x	4x	4x	—	—	—	—	died						
317a	0.50	1.3	4x	4x	4x	—	—	—	—	..	..	..	—	29—	42—	62—
316a	0.50	1.3	4x	4x	4x	..	x	—	..	—	9+	°	—	29—	42x	62x
312	0.50	1.3	4x	..	4x	—	—	—	—	—	..	—	..	23—	25—	
351	0.50	1.3	4x	..	4x	4x	4x	4x	—	—	—	—	—	50—	83—	107—
361	0.50	1.3	4x	..	4x	—	—	—	—	—	—	—	—25+	50x		
275	0.50	1.3	4x	4x	4x	4x	—+	—°	6—+	—	—+	°	°	30—	60—	90—
300	0.50	1.3	4x	4x	x	—	—	..	..	—°	—+	—°	—°	40—	70—	106—
315	0.50	1.3	4x	..	—	—	—	—	..	—	—+	—°	—	—	18—	
357	0.50	1.3	4x	..	4x	..	4x	—	—	—	—+	—	13+	16+—	79—	90—
183	0.50	1.3	4x	4x	4x	—+	—	—	—	—	..	—	—	—	32x	
447	0.60	1.6	4x	4x	2x	—	—+	—°	—+	—°	..	—	..	36—	40—	
446	0.60	1.6	4x	x	4x	—	—+	—°	—+	—°	..	—	..	36—	58—	435—
397	0.60	1.6	4x	4x	—	—	—+	—°	—+	—°	..	—	—	36—	58—	104—
438	0.60	1.6	4x	4x	4x	4x	4x+	—°	—+	—°	..	—	..	36—	40—	58—
364	0.75	2.0	4x	..	x	x	—	x	—	—	—	—	—	30—	41—	55—
369	0.75	2.0	4x	..	4x	—	—	—	—	—	—	—	—	41—	67—	144—
318	0.75	2.0	4x	4x	..	4x	—	6—+	—+	—°	..	—°	15+	20—		
314	0.75	2.0	4x	..	—	—	—	—	..	—	—+	—°	—	—	41—	50—
429	0.75	2.0	4x	4x	..	x+	—	6—+	—	—°	—+	—°	15+	19—+	30—	90—
316b	0.75	2.0	4x	..	..	x	—	6—+	—	—°	..	—	15+	19—+	30—	90—
700	0.77	2.0	4x	4x	4x	—	—	—	—	—	..	—	90—	120—	205—	
313	1.0	2.7	4x	—	—	..	—	..	..+	..	..	—	67—	80—		
321	1.0	2.7	4x	—	—	..	—	..	—+	..	..	—	52—	83—	102—	
198	1.0	2.7	4x	4x	4x	—	—+	..	..	—	..	—	54—	67—	90—	
449	1.0	2.7	4x	..	..	—+	—	6+	—	..	—+	—°	15+	19+	30—	
361a	1.0	2.7	4x	..	..	—+	—	6+	—	..	..	..	15+	19+	46—	
96	2.0	5.3	4x	4x	4x	—	—	..	..	—	..	—	28—	54—	67—	
			Effect of a Single Treatment													
463	2.0	5.3	4x	4x	x	—	..	—	..	..	..	—	37—	60—	74—	
445	3.0	8.0	4x	—	—	..	..	—								
481	4.0	10.7	4x	x	—											
489	5.0	13.3	4x	x	—	..	..	—								
436	6.0	16.0	4x	—	—											

* In these columns + indicates treatment; °, no treatment; 4x, actively motile Spirochaeta pallida; x, Spirochaeta pallida few and nonmotile; —, Spirochaeta pallida not found.

orchitis with or without gumma or chancre had developed and the aspirated fluid from the lesions showed actively motile spirochetes under the dark-field illuminator, the rabbits were considered suitable for the study. The age of the lesions varied from four weeks to two months. The severity and extent of the lesions varied considerably. In some cases the lesion presented itself as an initial stage of a generalized orchitis, or a chancre, in others the scrotum and testis were indurated and covered with a dry, gangrenous appearing crust and the scrotum was almost destroyed. Still, in some other cases the specific infection was associated with a pyogenic infection. The cases were selected to cover

from mild to severe lesions. Thirty-six syphilitic rabbits were treated by the intramuscular route, of which thirty-four received injections of water solutions and two received bismuth thioglycollate in sterile olive oil. As noted from table 1, the dosage varied between 0.25 and 6 mg. of metallic bismuth per kilogram of body weight. The number of treatments varied from one to ten. The intervals between successive treatments ranged from one to nine days, or averaged about three days. The lymph node transplants were made in some cases twice, one in middle of the course of treatment and the second after a complete course.

Spirocheticidal Effect.—The treated rabbits were examined about every day to determine the time necessary for permanent absence of spirochetes in the lesion. With few exceptions lesions were present on both testes. When the aspirated fluid from one testis became free from spirochetes, then the fluid from the other testis was aspirated, this being repeated every twenty-four hours until spirochetes were not found. The results of dark-field examinations on the aspirated fluid from both testes are summarized in table 2.

In table 2 are presented the results of dark-field examinations in coordination with the time of treatment. The examinations were carried on regularly for from fourteen to twenty-four days and then at irregular periods to the end of three months or over. Only those results have been presented here which have a bearing on the elucidation of the activity of bismuth thioglycollate as to (1) the size of dose, (2) the interval between treatments, (3) the number of treatments and (4) the rate of disappearance of spirochetes from the lesion. The dose varied between the subcurative dose of 0.67 mg. of bismuth thioglycollate per kilogram of body weight, the optimum curative dose of from 1.3 to 2.7 mg. and the well tolerated dose of 5.3 mg., and the apparently toxic doses of from 8 to 16 mg. per kilogram of body weight.

A treatment with the subcurative dose (0.67 mg. per kilogram) in some cases rendered the lesion temporarily free from spirochetes. After the recurrence of spirochetes as shown in table 2, doubling of the foregoing dosage promptly resulted in negative dark-field observations in rabbits 316, 317 and 319, in which the smaller dose did not have any further effect. Altogether, eleven rabbits were treated with 1.3 mg. of bismuth thioglycollate per kilogram of body weight. In one case after the first injection spirochetes were not found at the end of forty-eight hours. After the second injection only one rabbit still harbored spirochetes in the lesion at the end of forty-eight hours. A third treatment, on the fifth day, rendered the lesion free in the remaining rabbit. Therefore, it is noted that in 9 per cent of the cases one treatment of 1.3 mg. per kilogram rendered the lesion free in forty-eight hours. Twenty-four and forty-eight hours after the second treatment the lesions were free from spirochetes in 59 and 23 per cent of the cases, respectively. Thus,

in 91 per cent of the rabbits the lesions were free from spirochetes in four days with two treatments of 1.3 mg. of bismuth thioglycollate per kilogram of body weight.

Another group of eleven syphilitic rabbits received from 1.6 to 2.0 mg. of bismuth thioglycollate per kilogram. One injection gave negative dark-field observations in 18 per cent of the cases forty-eight hours after the treatment. Two injections rendered 36 per cent free from spirochetes twenty-four hours after the second dose and also 36 per cent

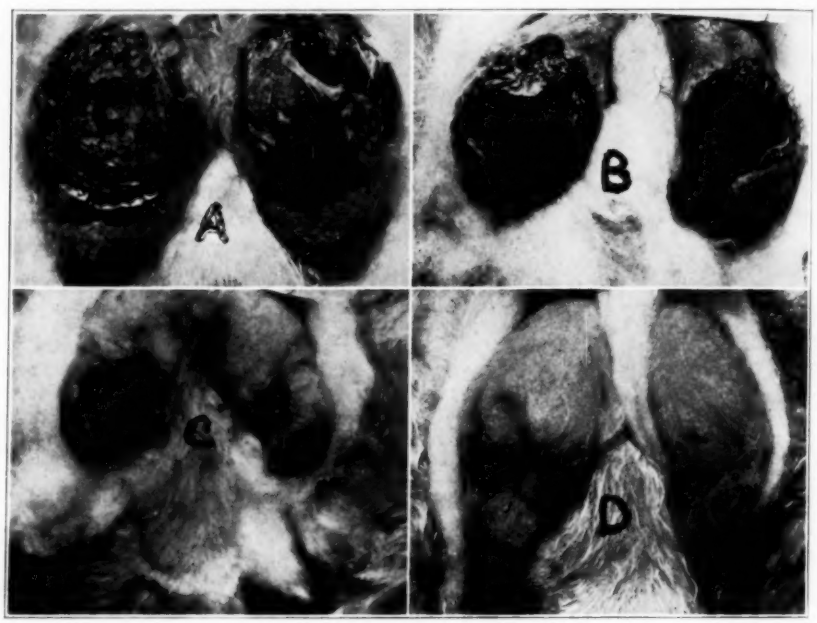

Fig. 4.—Involution of lesions following bismuth thioglycollate treatment; *A*, before treatment; *B*, after sixth treatment on fifteenth day, and *C*, after ninth treatment on the thirtieth day; dose 1.3 mg. per kilogram of body weight.

after forty-eight hours. Thus, two injections rendered 90 per cent of the rabbits' lesions free from spirochetes in four days.

With a higher dose, 2.7 mg. per kilogram, one injection rendered the lesions free in 40 per cent of the rabbits twenty-four hours after the treatment, and the remaining 60 per cent gave negative dark-field examinations twenty-four hours after the second injection; i. e., 100 per cent of the rabbits' lesions were free from spirochetes in three days with two injections.

A single injection of 5.3 mg. and over per kilogram was sufficient to render 100 per cent of the lesions free from spirochetes in from twenty-four to seventy-two hours.

From the study of the effect of different quantities of bismuth thioglycollate on *Spirochaeta pallida*, it appears that a dose of 0.67 mg. per kilogram is too small and subcurative. With twice and thrice the amount of such a dose, two treatments were required to render about 90 per cent of the lesions free from spirochetes in four days.

Involution of Lesions.—The rapidity with which the lesions involuted depended considerably on the extent of the original lesion. An extensive syphilitic lesion with a hard, indurated testis and with a hard, boardlike crust, as illustrated in figure 4, began to show softening and shrinking

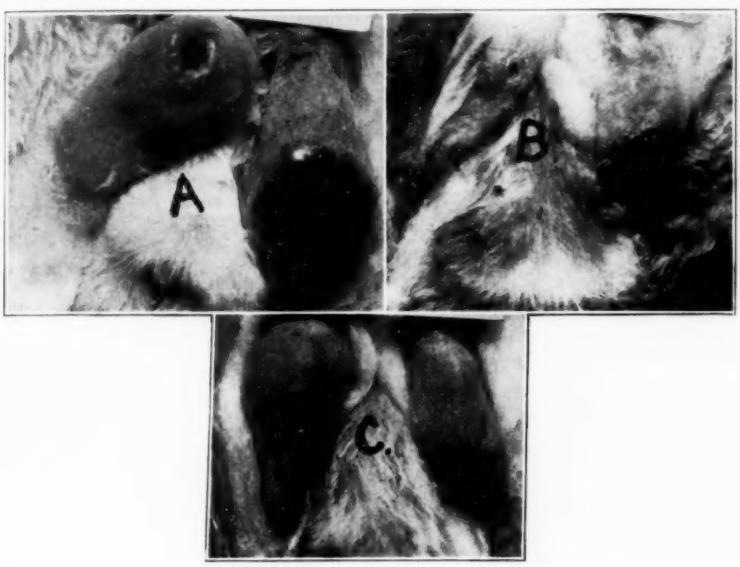

Fig. 5.—Involution of lesions following bismuth thioglycollate: *A*, before treatment; *B*, after fourth treatment on fourteenth day, and *C*, after fourth treatment on twenty-second day; dose 1.3 mg. per kilogram of body weight.

after the second injection. The improvement proceeded gradually and the testes were completely healed—one in twenty-five days and the other in thirty days with nine treatments of 1.3 mg. of bismuth thioglycollate per kilogram of body weight.

Less extensive lesions, as compared with the foregoing, involuted more rapidly with fewer treatments. Rabbit 360, as illustrated in figure 5, shows that the smaller lesion healed in fourteen days with four injections, and that the larger lesion, with the scab sloughed off and the testis protruding through the scrotum, healed in twenty-two days.

The rapidity with which lesions disappeared under treatment with bismuth thioglycollate is particularly well illustrated in figures 6 and 7, in case of rabbits 446 and 315, respectively. Rabbit 446 received five injections in a period of fourteen days. At the end of this period the

lesions were healed and the testes appeared normal. In the case of rabbit 315, the right testis presented considerable swelling and induration before treatment. The left testis was covered with an ulcer which extended through the scrotum and was adherent to the substance of the testis. The ulcer was covered with a black, boardlike, dry, gangrenous scab. With four injections of 1.3 mg. per kilogram of bismuth thioglycollate in ten days, the lesions presented a striking difference, compared with the original condition.

Curative Value.—Twenty-seven syphilitic rabbits were treated, of which eight received two or more courses of treatment; altogether thirty-six courses were given. At the completion of a course of treatment a lymph node transplant was made into a normal, healthy rabbit's testes. If the transplant rabbit did not develop a lesion within ninety days, it was assumed that the treatment had made the lymph glands innocuous and that the rabbit was probably cured. The technic and the methods of study were the same as reported previously with mercurosal [5] and bismuth salicylate.[6]

In table 3 are presented data showing the dose, the number of treatments, the presence or absence of a lesion and spirochetes in the treated and the transplant rabbits at the end of the observation period, the time of lymph node transplant following the course of treatment and, finally, the result of treatment—"cured" or "not cured." Under the term "cured" it is understood that the treated and the lymph node transplant rabbits did not show lesions or spirochetes at the end of the observation period. "Not cured" indicates the presence of either a lesion or spirochetes in the treated or lymph node transplant rabbit.

A group of three syphilitic rabbits was treated with 0.25 mg. of bismuth per kilogram of body weight. As noted from table 3, the lesion and the spirochetes did not disappear during a course of eight injections. This undoubtedly strongly suggests that 0.25 mg. of bismuth in the form of soluble bismuth thioglycollate salt is not sufficient to saturate the body with bismuth.

When the foregoing group of rabbits was placed on double the dose given previously (0.5 mg. of bismuth per kilogram), the spirochetes disappeared from the lesion in the same time as if these rabbits had not been treated before. Of eleven rabbits treated with 0.5 mg. of bismuth per kilogram of body weight, only three rabbits apparently were cured, six were not cured and two were doubtful as to cure; i. e., in this group from seven to ten injections every second to fourth day contained too little bismuth to produce cures in 70 per cent of the animals. Increasing the dose to 0.6 mg. of bismuth per kilogram raised the percentage of

5. Gruhzit, O. M.: Mercurosal in Experimental Rabbit Syphilis, Arch. Dermat. & Syph. **11**:509 (April) 1925.

6. Gruhzit (footnote 1, fourth reference).

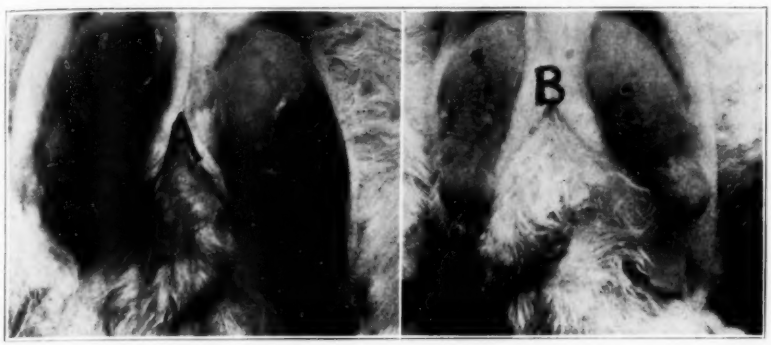

Fig. 6.—Involution of lesions following the bismuth thioglycollate treatment: *A*, before and *B*, after, the fifth treatment on the fourteenth day; dose 1.3 mg. per kilogram of body weight.

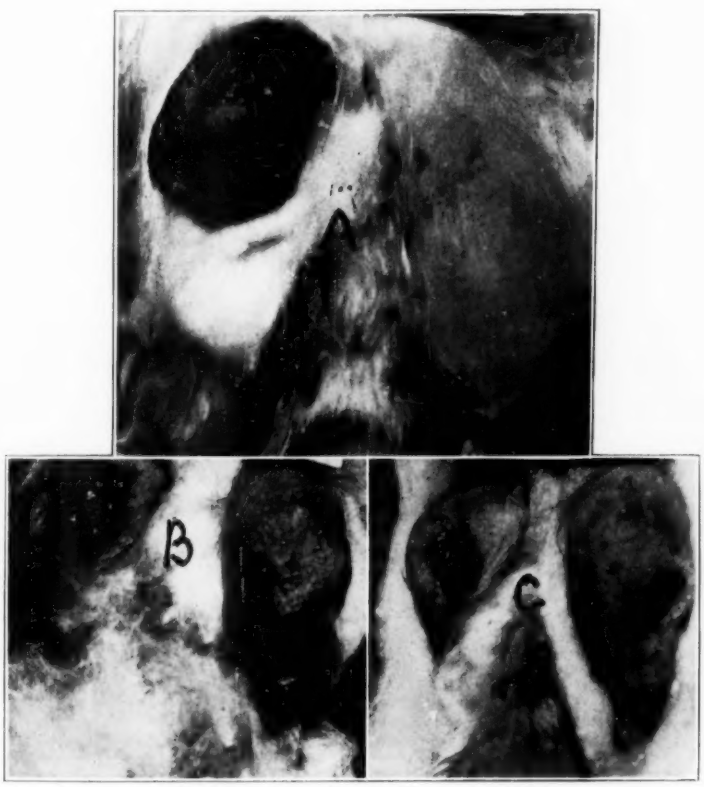

Fig. 7.—Involution of lesions following the bismuth thioglycollate treatment. *A*, *B* and *C*, respectively, before the treatment and after the fourth injection, on the tenth day, and the sixth injection on the fifth day; dose 1.3 mg. per kilogram.

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"cures" to 50. A dose of 0.75 mg. of metallic bismuth per kilogram given to a group of nine rabbits over a course of from six to ten treatments about every second to fourth day produced a "cure" in 100 per cent of the cases. A dose of 1 mg. of bismuth per kilogram injected from six to eight times rendered the lymph nodes sterile, as none of the transplant rabbits developed a lesion.

TABLE 3.—*Curative Value of Bismuth Thioglycollate*

Rabbit	Dose, Mg. Bismuth per Kg.	Number of Injections	Treated Rabbits		Lymph Node Transplanted Rabbits		Results
			Lesion	Spirochetes	Lesion	Spirochetes	
319	0.25	8	Present	Positive	.....	.....	Not cured
	0.50	3	None	None	None	None	Cured
316	0.25	7	Present	Positive	.....	.....	Not cured
	0.50	8	Present	Positive	Present	Positive	Not cured
	0.75	7	None	None	None	None	Cured
317	0.25	7	Present	Positive	.....	.....	Not cured
	0.50	8	None	None	None	None	Cured
312	0.50	10	None	None	None	None	Doubtful
351	0.50	10	None	None	Present	Positive	Not cured
	0.60	3	None	None	Present	Positive	Doubtful
361	0.50	10	Present	Positive	Present	Positive	Not cured
	1.0	6	None	None	None	None	Cured
315	0.5	7	None	None	None	None	Cured
275	0.5	10	None	None	Present	Positive	Not cured
360	0.5	10	None	None	None	None	Cured
357	0.5	9	None	None	Present	Positive	Not cured
183	0.5	9	Present	Positive	Present	Positive	Not cured
397	0.6	10	None	None	Present	Positive	Not cured
	0.75	8	None	None	None	None	Cured
438	0.6	10	None	None	None	None	Cured
	0.75	8	None	None	None	None	Cured
447	0.6	10	None	None	Present	None	Not cured
446	0.6	10	None	None	None	None	Cured
	0.75	6	None	None	None	None	Cured
364	0.75	10	None	None	None	None	Cured
339	0.75	10	None	None	None	None	Cured
314	0.75	7, 9	None	None	None	None	Cured
429	0.75	6	None	None	None	None	Cured
700	0.77	9	None	None	None	None	Doubtful
313	1.0	8	None	None	None	None	Cured
321	1.0	8	None	None	None	None	Cured
198	1.0	8	None	None	None	None	Cured
449	1.0	6	None	None	None	None	Cured
96	2.0	3	None	None	None	None	Cured
463	2.0	1	None	None	None	None	Cured
300	4.5	1	None	None	None	None	Cured

TABLE 4.—*Correlation of Dosage of Bismuth to the Number of Treatments and to the Incidence of "Cure"*

Number of Rabbits	Dose, Mg. Bismuth per Kg.	Average Number of Treatments	Cured, per Cent	Not Cured, per Cent
3	0.25	7.3	0.0	100.0
11	0.50	8.5	30.0	70.0
4	0.60	10.0	50.0	50.0
9	0.75	7.0	100.0	0.0
5	1.00	7.2	100.0	0.0
1	2.00	1.0	100.0	0.0
1	2.00	3.0	100.0	0.0
1	4.50	1.0	100.0	0.0

A single dose of 2 mg. and over of bismuth per kilogram appeared to be sufficient to render the lymph nodes innocuous to normal rabbits.

It is apparent from the study of bismuth thioglycollate that it possesses considerable spirocheticidal activity in doses of 0.5 mg. of bismuth

per kilogram of body weight, but that an optimum curative action is obtained when the dose is increased to 0.75 mg. of bismuth per kilogram of body weight.

Clinical Experience.—A limited number of patients have been treated with bismuth thioglycollate to ascertain its action on human beings. In particular, the attempt was made to study its tolerance, its cumulative action, the effect on the kidneys, the influence on the Wassermann reaction and the healing effect on the syphilitic lesions.

Seventeen patients were treated. Brief histories are presented to elucidate on the points mentioned above.

REPORT OF CASES

CASE 1.—Mrs. B., aged 37, a white American woman, divorced, had not had any pregnancies, and gave no history of an initial lesion, but she said that she had had some "female trouble" sixteen years before. On examination, Feb. 5, 1926, a squamous palmar syphilid was seen on the right hand. Other lesions were not noted. The Wassermann reaction, February 9, was 4 plus. Bismuth thioglycollate treatment was administered intramuscularly (0.1 Gm.) every other day for sixteen injections. Other treatment was not given. On March 11, the lesions had disappeared entirely. The Wassermann reaction was negative. On May 3, new lesions or a recurrence were not observed. The Wassermann reaction was still negative. The urine, examined weekly, did not show albumin at any time. Pain and lumps were not present at the site of injection.

CASE 2.—Mrs. R., aged 36, a widow, who had been a school teacher for eleven years, presented an aortic aneurysm without the history of an initial or secondary lesions. There had been several abortions at from two to four months. On February 26, the Wassermann reaction was 4 plus. Sodium iodide intravenously and bismuth thioglycollate were administered biweekly for twenty injections. There was considerable improvement in the general condition. The blood Wassermann reaction on May 15 was plus-minus. On June 5, the Wassermann reaction was negative. The injections did not produce pain or lumps. Darkening of the gums and gastro-intestinal symptoms were not noted. The urine remained free from albumin.

CASE 3.—Daisy B., a colored woman, aged 27, presented herself on January 26, with a generalized papular eruption. The Wassermann reaction was 4 plus. Eight injections of arsphenamine and twelve of mercury caused the rash to fade markedly in six weeks. March 15 the Wassermann reaction was still 4 plus. Bismuth thioglycollate 0.1 Gm. was administered biweekly from March 15 to May 15 in a total of sixteen injections. The Wassermann reaction on May 20 was negative. The eruption disappeared promptly under bismuth thioglycollate treatment.

CASE 4.—Mrs. H., aged 30, white, an American, a widow with one child, had had, previous to bismuth thioglycollate, twenty arsphenamine, fifty mercury, and twenty bismuth salicylate injections and considerable potassium iodide. The case was one of latent tertiary syphilis with a fixed positive Wassermann reaction. Bismuth thioglycollate, 0.1 Gm., was administered at forty-eight hour intervals for sixteen injections. The patient did not show signs of local reaction at any time. At the end of the course the patient presented a marked bluish

line on the gums and complained of a sore mouth with a decided inflammatory buccal mucous membrane. The Wassermann reaction was still 4 plus. The urine did not show albumin at any time.

Cases 5, 6, 7, 8, 9 and 10.—The patients had been on a routine arsphenamine and mercury treatment for two courses without a change in the Wassermann reaction. Following this, bismuth thioglycollate, 0.1 Gm., was administered three times a week for five weeks (sixteen injections). The Wassermann reaction was negative in all cases one week after completion of the course and has remained negative since. In four other cases similar to the six just described the Wassermann reaction remained positive one and four weeks after a course of bismuth thioglycollate injections.

Cases 15 and 16.—Two patients with latent tertiary syphilis with Wassermann-fast reaction who had received, in addition to arsphenamine and mercury, bismuth salicylate, were given bismuth thioglycollate biweekly for five weeks without change in the Wassermann reactions.

Case 17.—Mrs. B. received one injection intramuscularly and complained almost immediately of a severe burning sensation, which lasted for twenty-four hours.

In this series, more than 260 injections of 0.1 Gm. of bismuth thioglycollate in 1 cc. of distilled water were given deep intramuscularly in the thigh or in the arms. Pain did not appear in any but one patient (at one injection). It is possible that in this one case the injection was made in or near a nerve trunk. These patients did not develop lumps, except when the injection was given in the arm, and then they were small and painful only on pressure.

In one patient out of sixteen a distinct darkening of gums was noted. This is of interest as it brings out the fact that it is possible to bring the patient to a point of saturation with bismuth thioglycollate and yet to avoid a toxic action. The fifteen remaining patients did not develop at any time darkening of the gums or gastro-intestinal disturbances.

The kidneys in the sixteen patients who received 0.1 Gm. of bismuth thioglycollate twice or thrice weekly in a course of from sixteen to twenty injections probably remained unaffected, as albumin did not appear in the urine at any time.

Secondary and tertiary lesions were influenced rapidly. In case 1, a palmar syphilid, the lesions dried up and receded after three intramuscular injections within one week, and after sixteen injections the patient did not present any clinical symptoms (spinal fluid not examined) and the Wassermann reaction had become negative.

The Wassermann reaction was changed to negative after one course with bismuth thioglycollate in one case of palmar syphilid and one case of aortic aneurysm. In six cases one course of bismuth thioglycollate changed the reaction to negative when two courses of arsphenamine and mercury had not had any effect. In four cases in which similar treatment was given the Wassermann reaction was not influenced. In three cases

Wassermann-fast to arsphenamine, mercury and bismuth salicylate, the bismuth thioglycollate did not have any effect on the Wassermann reaction. It would appear from this study that bismuth thioglycollate has probably a better action on the Wassermann reaction than arsphenamine and mercury, but that this effect is probably not greater than that of bismuth salicylate or any bismuth compound.

COMMENT

The work on bismuth thioglycollate was undertaken in order to find a substance which could be injected intramuscularly in water solution without causing injury to the tissues and which would not form insoluble deposits at the site of injection. Gruhzit [6] has shown that the potassium bismuth tartrate is corrosive in action and is precipitated at the site of injection as an insoluble bismuth salt and is retained there for variable periods of time, exceeding over fifty days. On the contrary, bismuth thioglycollate remains as a water soluble substance and inside of two hours is entirely absorbed and distributed, through the whole body.

The constant fear of cumulative action of the present bismuth salts in vogue in the treatment of syphilis [7] was an additional incentive for a preparation of a soluble bismuth compound, the activity of which could be guided as readily as that of arsphenamine.

The minimum lethal dose of bismuth thioglycollate intravenously and intramuscularly ranges between 9 and 12 mg. of bismuth per kilogram. According to Kolle [8] the minimum lethal dose of potassium bismuth tartrate, intravenously, is 4.5 mg. of bismuth per kilogram. The curative dose of bismuth thioglycollate is from 1.5 to 2 mg. of bismuth, while that of potassium bismuth tartrate when used in water solution is 3 mg. of bismuth per kilogram of body weight.

It is indicated from these comparisons that bismuth thioglycollate is only about one half to one-third as toxic and about twice as efficient a spirocheticide as the tartrates.

The study of spirocheticidal and curative values of bismuth thioglycollate indicates that a dose of 0.25 mg. of bismuth per kilogram did not have a therapeutic value. A dose of 0.5 mg. of bismuth appeared curative in only 30 per cent of cases. The increase of the dose to 0.6 and 0.75 mg. per kilogram increased the curative value to 50 and 100 per cent, respectively. It is therefore suggested that the optimum dose of bismuth in the form of bismuth thioglycollate is about 0.75 mg. of bismuth per kilogram body weight. These conclusions are arrived at also indirectly in the study of the elimination of this compound. Analyses of the

7. Cole (footnote 1, first reference).

8. Kolle, W.: Die Chemotheraputische Studien über Wismut, Med. Klin. **20**:1097, 1924.

excreta of dogs treated with 0.5, 0.75 and 2.8 mg. of bismuth per kilogram show that the elimination in first forty-eight hours is 40, 17 and 19 per cent of bismuth, respectively. At the end of seventy-two hours the excreted bismuth in these dogs was respectively 40, 23 and 21 per cent. It would appear that unless the dose of 0.5 mg. of bismuth per kilogram is given about every forty-eight hours, it would be a difficult matter to maintain the body in a bismuth saturated condition. But with 0.75 mg. of bismuth per kilogram was injected, namely, 2.5 and 2.4 mg. reached, even if given only once in seventy-two hours. This probably is explainable because the total bismuth eliminated in seventy-two hours was about the same whether a small dose of 0.5 mg. or a larger one of 0.75 mg. of bismuth per kilogram was injected, namely, 2.5 and 2.4 mg. of bismuth, respectively, from each dog.

The clinical experience with bismuth thioglycollate, though limited at present to only seventeen cases, supports the experimental observations on syphilitic rabbits. Under this treatment the lesions heal readily, and the Wassermann reaction is influenced rapidly and permanently. It causes little or no pain or lumps at the site of injection. The greatest advantage of bismuth thioglycollate is that it remains water soluble when injected into the body. It does not form insoluble albuminates at the site of injections and is not precipitated as metallic bismuth. It diffuses rapidly through the system. It saturates patients readily without producing a cumulative toxic effect. From 20 to 40 per cent of it is eliminated in the first seventy-two hours and to keep the patient in a saturated state the drug should be given three times a week in doses of 1.3 mg. per kilogram of body weight, or twice a week in doses of 2.0 mg. per kilogram.

SUMMARY

1. A soluble bismuth compound of thioglycollic acid has been prepared and studied in experimental and clinical syphilis.

2. Its toxicity to animals is about 29 mg. of bismuth thioglycollate per kilogram, intramuscularly, and about 23 mg. per kilogram, intravenously. The tolerating dose is from 16 to 24 mg. per kilogram of body weight. The treatment dose is between 1.3 and 2.5 mg. per kilogram.

3. Bismuth thioglycollate does not produce any injury, beyond some Zenker's necrosis at the site of injection, as compared with severe necrosis produced by potassium bismuth tartrate in water or oil suspensions.

4. Albuminuria was not produced either in experimental animals or in clinical experience by doses of from 1.3 to 2 mg. of bismuth thioglycollate per kilogram.

5. The blood urea nitrogen was not affected in a course of ten injections, with a dosage of from 1.3 to 2 mg. per kilogram. When the

dosage was increased to 7.5 mg. per kilogram, transient blood urea retention was produced.

6. Histologic studies indicated that a dose of 2.6 mg. per kilogram did not show any changes in the liver, spleen and kidneys. Distinct injury to the cells of various organs was noted when a dosage of 5.2 mg. per kilogram was used. The injury appeared greater in the kidney than in the liver, which suggests that bismuth thioglycollate is more nephrotoxic than hepatotoxic.

7. Bismuth thioglycollate is absorbed from the site of injection in less than two hours. About 20 to 40 per cent of bismuth appears in the urine and feces within seventy-two hours. The greatest part of it is eliminated through the kidneys.

8. The spirocheticidal value increases with the quantity of the drug given. The minimum effective dose is about 1.3 mg., while the optimum spirocheticidal dose is from 2 to 2.5 mg. per kilogram.

9. Syphilitic rabbits treated in a course of from seven to ten injections rendered lymph nodes innocuous to normal rabbits in 30, 50 and 100 per cent of the cases with a respective dosage of 1.3, 1.6 and 2.0 mg. per kilogram of body weight.

10. A limited clinical experience indicates that bismuth thioglycollate produces a somewhat more rapid improvement in lesions than do the insoluble bismuth compounds. It does not cause any lumps or pain at the site of injection when administered in water solution. The patient can be saturated readily without danger of cumulative action. The Wassermann reaction was influenced rapidly.

THE ACNE BACILLUS

VARIATIONS IN THE CULTURAL AND MORPHOLOGIC CHARACTERISTICS *

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In an article entitled "The Cultural Requirements of the Acne Bacillus," etc., Ketron and Burky [1] briefly described an organism occurring as a contaminant in three of ten strains of the acne bacillus which they were studying at that time. In one instance the organism grew out with the acne bacillus, following the implantation of a seborrheic filament on an agar slant, and in two instances after the contents of acne papules had been planted in the same manner.

Its cultural characteristics, in general, resembled those of the acne bacillus, but it differed considerably from their strains of this organism in its rapidity of growth and, under certain conditions, in its morphology.

The present work deals with a study of this bacillus and, since its cultural requirements and habits are similar to those of the acne bacillus as it is usually described, it will be regarded as a variety of the acne bacillus and referred to as acne *B*. The organism which we have previously studied, the one which is believed to be the acne bacillus of the majority of previous investigations, will be referred to as acne *A*.

SOURCE OF MATERIAL AND METHOD OF OBTAINING CULTURES

Cultures were taken from thirty-five patients, most of whom had seborrhea or acne and seborrhea combined. Cultures from seborrheic filaments, all from different patients, yielded acne *B* in twelve of twenty-two cases. Cultures from acne papules or nodules showed acne *B* in one of thirteen cases. Cultures from six acne pustules from five cases gave negative results. Cultures from five comedones from five patients yielded the organism in one case. Scales from the scalps of thirteen patients with seborrhea and pityriasis capitis gave positive results in two instances of the former disease.

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* From the Departments of Dermatology, Pathology and Bacteriology, Johns Hopkins Medical School.

* Read at the Golden Anniversary Meeting of the American Dermatological Association, Philadelphia, May, 1926.

1. Ketron, L. W., and Burky, E. I.: Cultural Requirements of Acne Bacillus with Special Reference to Hydrogen Ion Concentration of Mediums Most Suitable for Its Growth, Arch. Dermat. & Syph. **11**:354 (March) 1925.

Scales from two cases of exfoliative dermatitis were negative. In one case of psoriasis, a culture taken from the back yielded the organism, but one taken from the arm was negative. Its presence in the former was most likely due to the coexisting seborrhea.

In making the cultures, filaments, comedones, contents of acne lesions or scales were macerated in a tube of sterile salt solution and deep shake tubes of a 1 per cent dextrose infusion agar (p_H 6.8) were inoculated with increasing dilutions of this material.

After being incubated for from one to two weeks at 37 C., cultures were considered positive for acne *B* when they showed one or more large pinkish colonies which usually stood out in striking contrast to the much more numerous and smaller colonies of the acne *A* bacillus

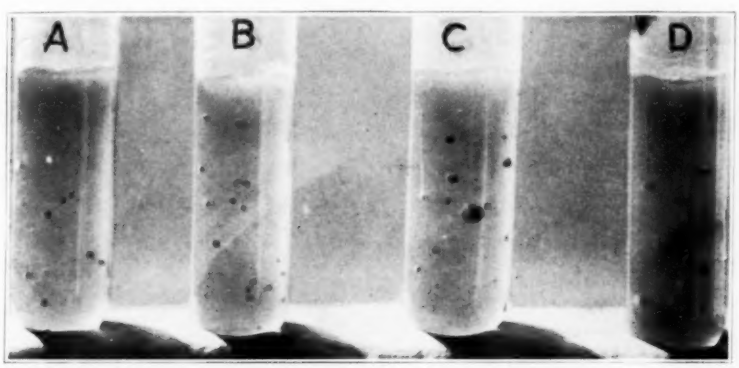

Fig. 1.—Shake tube cultures of seborrheic filaments from four cases; tubes *A* and *B* show only acne *A* colonies; tube *C* shows one acne *B* colony, and in tube *D* the majority of the colonies are of the *B* variety.

(fig. 1). The accuracy of this criterion for differentiation was supported by microscopic examination and later, in some cases, by the cultural characteristics. The acne bacillus *B* was never found apart from the acne *A* variety, although in some instances this statement is based solely on macroscopic examination of the colonies. The number of the acne *A* colonies was usually far in excess of that of the *B* variety. In one case of seborrhea, however, several cultures made at different times from nose filaments yielded acne *B* almost exclusively. Staphylococci were seldom encountered in cultures from nose filaments, provided the nose had previously been well scrubbed with alcohol. In comedones, however, they were always present, but they seldom occurred in acne papules or nodules which did not give any clinical evidence of free pus and from which only a gelatinous granular material could be expressed after incision.

CULTURAL CHARACTERISTICS.

Ten strains of acne *B* were employed and the technic in transplanting and growing the organism was similar to that already described for the cultivation of acne *A*.[1] It was found necessary to plant a rather large amount of material in order to obtain good vigorous growth, much more being required for aerobic than for anaerobic cultivation.

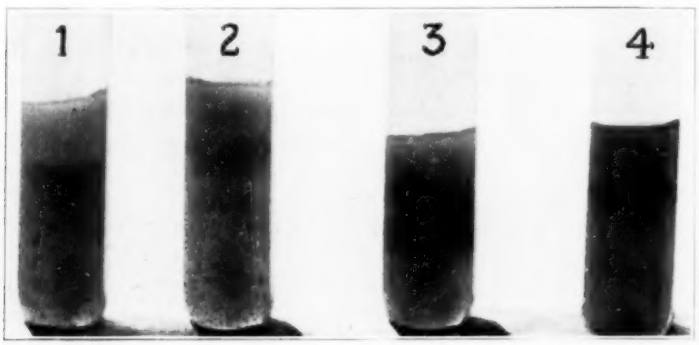

Fig. 2.—Tube 2 shows the characteristic zone development of acne *A* which does not occur in acne *B*, as illustrated in tube 1; in tubes 3 and 4 are seen unusual restriction of growth of acne *A*.

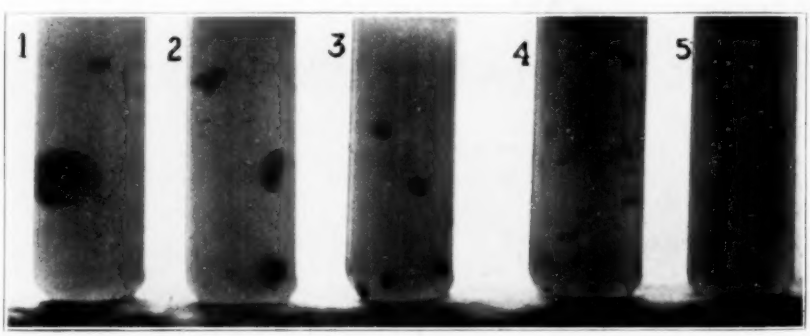

Fig. 3.—Tubes 1 and 2 show unusually large acne *B* colonies; tube 3 shows the average size of acne *B* colonies after ten days' incubation. Comparison may be made with ten-day old cultures of acne *A* in tubes 4 and 5.

The organism grew best on acid mediums, and all agar and broth were made with a reaction near p_H 6.8. A small amount of growth could occasionally be obtained anaerobically on the usual laboratory mediums having reactions ranging around p_H 7.6. It was very scanty, however, and did not show pigmentation. Comparatively little growth occurred on agar or broth without the addition of sugar. For this reason 1 per cent dextrose was added to these mediums for routine cultivation.

1. *Agar* (2 per cent meat infusion agar, plus 1 per cent dextrose, p_H 6.8. This was used both for slants and deep shake tubes).—(*a*) Shake tubes. The growth is usually visible after forty-eight hours at 37 C., extending from a depth of 0.5 to 1 cm. below the surface of the medium to the bottom of the tube. There is no clear band under the upper zone of growth such as is characteristic of acne *A*, but development takes place with equal rapidity throughout the entire anaerobic portion of the tube, although occasionally the colonies appear to be thicker in the upper 0.5 cm. (fig. 2). In the tubes of high dilution, in which only a few colonies are present, growth takes place rather rapidly, the colonies reaching a diameter of from 2 to 4 mm. or more in from one to two weeks' time (fig. 3). They may appear as either single biconvex or compound disks. The color varies from a light pinkish or brownish tint to a deeper pink or coral, the light pigmentation being more common than the heavier shades.

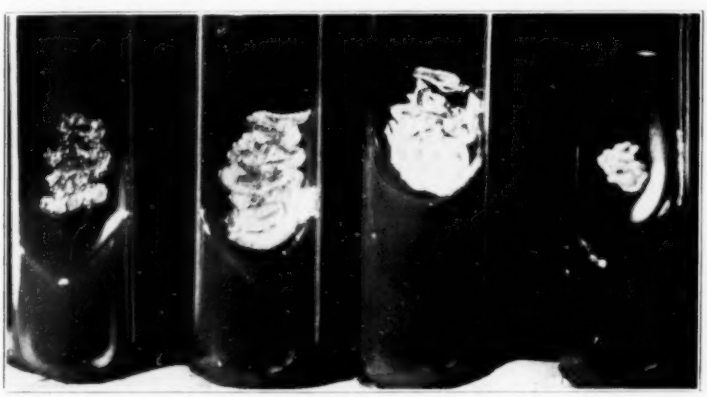

Fig. 4.—Anaerobic cultures of acne bacilli on 1 per cent dextrose agar; the two tubes on the left show the *B* variety, and the two on the right the *A* variety.

(*b*) *Slant agar:* With anaerobic cultivation at 37 C. good growth may be obtained in three or four days, which usually reaches a maximum in six or eight days. It is abundant, confluent and moderately raised, with usually a beaded or irregular surface which is at first moist. As the cultures become older, the growth becomes dryer, often crumbly, and frequently develops a metallic luster. The edge is then thin, gradually sloping down from the thicker portions, and may be finely scalloped. The color varies from a light pink or gray to a deep pink or coral (fig. 4). With aerobic cultivation the transplanted material usually has a soft, putty-like consistency, is heaped up and is grayish or pinkish, similar to the color found in acne *A*. At times, however, there is some tendency to dryness.

2. *Broth* (Meat infusion broth plus 1 per cent dextrose, p_H 6.8).—Anaerobically, at 37 C., a good growth may be obtained in from three to six days. There is usually a heavy, granular or slightly ropy sediment on the bottom of the tube with a clear or almost clear supernatant fluid. In most of the cultures also there is a fairly heavy deposit on the sides of the tube. This extends, at times, almost to the top of the broth, particularly when the tube has occupied a slanting position in the anaerobic jar. Moderate growth may be obtained aerobically with heavy inoculation.

3. *Fermentation Tubes* (Meat infusion broth plus 1 per cent dextrose, p_H 6.8 in Smith tubes).—After one week's incubation at 37 C. all strains showed a heavy sediment in the neck of the tube which extended up into both bulb and arm, with the exception of strain 3, growth of which was slight. The height of the deposit in the closed arm varied, extending all the way to the top in one instance. Only two strains showed a general clouding of the broth. In some instances large granules were floating in the fluid near the top of the closed arm. Gas was not formed.

4. *Litmus Milk* (Cultures incubated twenty-four days at 37 C.).—Anaerobically, seven strains showed acid formation. One formed a soft curd without heating, while the other six coagulated when heated. The remaining three strains did not show acid formation and did not coagulate when heated. Aerobically, growth occurred more slowly, but the end-results were similar to those obtained in the anaerobic series.

5. *Loeffler's Medium.*—When first tested on this medium, under anaerobic cultivation, in a large jar, only one strain showed visible growth, although control tubes on dextrose agar grew well. Later, two strains were cultured, in which the individual tubes were made anaerobic separately by the Wright method, and good development occurred in two weeks' time. The growth was whitish, smooth and moist in appearance, but after standing two more weeks at room temperature, it became dryer, with a moderately developed metallic sheen.

6. *Gelatin.*—Growth did not occur at 20 C. after thirty days. When incubated at 37 C., however, a moderate development occurred in the lower portions of the tubes, but the medium solidified when placed in the ice chest.

7. *Potato.*—Anaerobically, only scanty growth was obtained, but quite deep pink or red pigmentation developed.

8. *Fermentation Reactions.*—The fermentation reactions of ten strains of acne *B* and five strains of acne *A* were tested with nineteen substances. After several preliminary trials, it was found that more satisfactory results could be obtained with a solid medium than by using broth. The various test substances were added to a sugar-free infusion agar in 1 per cent concentration, and bromcresol purple was used as the indicator. The hydrogen ion concentration of the medium was p_H 6.8. Deep shake tubes were inoculated with 0.1 cc. of a heavy broth culture of the various strains. The acne *B* strains were incubated for from two to four weeks and the acne *A* strains for ten weeks. The amount of growth corresponded closely with the degree of fermentation. Controls, and the tubes containing the unfermented substance, showed little or no demonstrable growth.

As will be seen in the table, there was some variation of the fermentation reactions between the different strains of each group, as well as a group variation. In acne *B*, changes in the color of the indicator proceeded rapidly in the materials most easily fermented. In all strains except one a pronounced fermentation occurred in levulose after three days and the fermentation in glycerol was almost as far advanced. After two weeks' incubation the hydrogen ion concentrations of the levulose and dextrose cultures were determined. The reactions varied between p_H 4.8 and 5.8, with the exception of strain 9 *C* which gave a reaction of p_H 6.2 in levulose.

The remaining strains were incubated for four weeks. All of them fermented glycerol giving p_H values ranging from 4.8 to 5.4. Saccharose was fermented by all strains except *2d* which gave a p_H value of 6.9. (This was repeated and slight fermentation resulted with a p_H of 6.3.) Maltose and galactose were more slowly attacked, but were fermented by all strains. Irregular results were encountered in raffinose and mannite, and some slight fermentation of dextrin and starch occurred.

In cultures of acne *A*, fermentation proceeded more slowly. After one week, three strains showed moderate fermentation of levulose, with beginning changes in sorbitol, dextrose, galactose and glycerol. After three weeks, fermentation by all but one strain was complete—i. e., the indicator had turned completely yellow—in levulose, dextrose and sorbitol.

*Fermentation Reactions**

Acne B Strains	Levulose	Glycerol	Dextrose	Saccharose	Raffinose	Maltose	Galactose	Mannite	Dextrin	Starch	Adonitol	Sorbitol	Lactose
1	3	3	3	3	0	3	2	0	0	1	...	...	...
2d	3	3	3	0	0	2	2	0	0	0	...	...	...
3	3	3	3	3	0	2	2	3	1	0	...	...	...
4b	3	3	3	3	3	3	2	0	0	0	...	...	...
5	3	3	3	3	3	2	2	0	0	0	...	...	...
6	3	3	3	3	3	3	2	3	1	2	...	...	...
8	3	3	3	3	3	3	2	0	1	2	...	...	...
9c	2	3	3	3	1	2	1	0	1	0	...	...	...
14	3	3	3	3	0	3	2	3	1	0	...	...	...
16	3	3	3	3	3	3	2	0	2	2	...	...	...
Acne A Strains													
A	3	3	3	0	0	0	2	3	0	0	0	3	2
G	3	2	3	0	0	0	2	2	0	0	1	3	0
M	3	3	3	3	0	0	2	3	0	0	3	3	2
R	3	0	3	0	0	2	2	3	0	0	2	0	0
Y	3	3	3	3	0	0	3	3	0	0	3	3	3

* Negative results were obtained in arabinose, dulcitol, inulin, rhamnose, salicin and xylose which are not recorded in the table. Deep agar shake tubes, p_H 6.8, containing 1 per cent of the test substances, were used with brom cresol purple as the indicator. The degree of fermentation is indicated by the numerals 1, 2 and 3; 1 indicates a slight change in the color of the indicator; 2, partly brownish or yellowish; 3, all of indicator yellow.

In the results, after ten weeks' incubation, considerable variation will be noted. Levulose, dextrose, galactose and mannite were fermented by all strains of acne *A*, the latter two less completely and much more slowly than the former two. Sorbitol and glycerol were well fermented by all strains except *R*. It had been noticed in previous studies of ten strains of acne *A* that sorbitol was rapidly utilized by these organisms.

MORPHOLOGY

Gram's stain was found to be the most valuable stain for studying the variations in morphology of the organism. Methyl violet *B* is preferable to gentian violet in making the stain. When the latter dye is used, the irregular staining, to be described later, is not marked, since the whole organism usually stains, but with methyl violet the

proper differentiation is obtained. With this stain the organism is weakly gram-positive in the older cultures, and in order to avoid complete decolorization of most of the bacilli, it is necessary to use alcohol for only a short time.

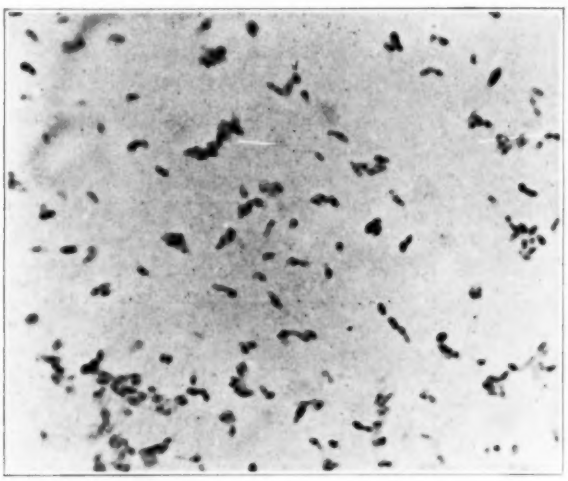

Fig. 5.—Acne *B* from a ten-day old anaerobic culture on 1 per cent dextrose agar. × 1,100.

Fig. 6.—Drawing of "plasma cell" forms from a smear of strain 2 of the acne bacillus *B*; nearly all of the organisms were of this character.

In the youngest anaerobic cultures—about forty-eight hours old—in which growth is apparent, acne *B* is a nonmotile, gram-positive bacillus, varying in size from 6 to 8 microns in diameter by 1 to 1.5 microns in length, some strains being somewhat larger than others.

The organism at this age stains evenly, has rounded ends and may be either straight or slightly curved. It occurs singly and in pairs, and small groups or short chains are common. The bacillary forms are fairly regular in contour, but coccoid, oval, wedge-shaped or other types may be encountered.

In cultures from one to two weeks old, considerable irregularity in morphology and staining is usually observed. This becomes more marked as the cultures grow older, although in some strains variations in morphology are not so pronounced as in others. One of the most common forms encountered is an oval or round cell, faintly colored by the counterstain, with a deeply staining granule in one end. The location of the granule and the general contour of the organism

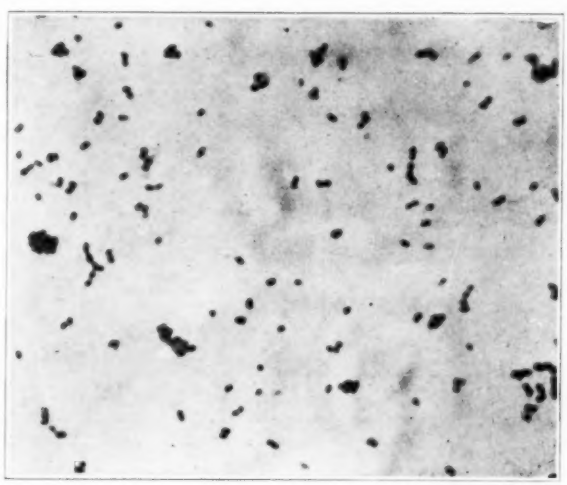

Fig. 7.—Two weeks old broth culture of acne *B.* × 1,100.

resembles a miniature plasma cell. These forms vary in size from 0.5 to 2 microns in width. Other variations of this character are also seen. The granule may be in the center of the cell, which may have an oat shape with pointed ends, or ends which diverge in fan shape. In some cases there may be two central granules lying transversely or longitudinally across the organism, resembling cellular mitotic division [2] (figs. 5 and 6). Small groups with columnar-shaped cells, which have central granules and lie parallel to each other, are occasionally seen. These organisms are smaller than the young bacillary forms and resemble minute columnar epithelium. Evenly stained ovoid, coccoid, bottle, wedge, dumb-bell and club shapes, as well as forms resembling

2. For the purpose of description, these faintly staining cellular forms with deeply staining granules will be referred to henceforth as plasma cell forms.

the younger organisms already described, may also be present. Long bacillary organisms may be more or less prominent at times, occasionally attaining a length of 5 or 6 microns. These may be very slender or quite thick and swollen in appearance. They stain either intensely

Fig. 8.—Acne *B* on Loeffler's medium. × 800.

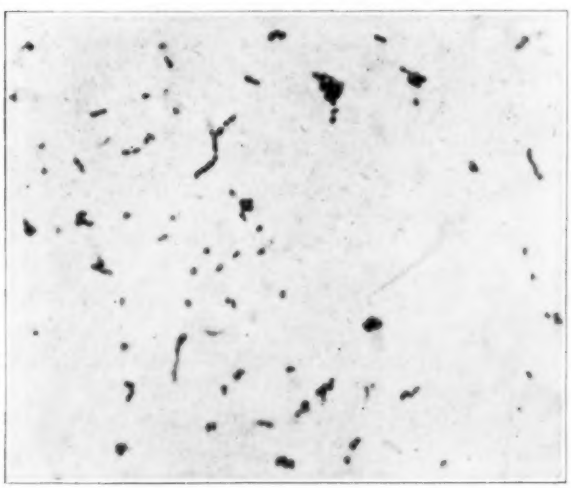

Fig. 9.—Ten-day old aerobic culture of acne *B* on 1 per cent dextrose agar. × 1,100.

black or irregularly with gram-positive granules, or have gram-positive and gram-negative sections.

Some strains show the coccoid and plasma cell forms to a more marked degree, while in others the bacillary forms may predominate.

In 1 per cent dextrose infusion broth, the organism is frequently slightly smaller than on agar (fig. 7). In some cases short bacillary or coccoid forms are the most common, but occasionally longer bacilli dominate the picture. These occur singly, in small masses or in chains varying from two to eight or ten cells. The chains may be made up of short bacilli, or of coccoid forms indistinguishable from streptococci. Plasma cell forms also are usually present.

Only two strains were studied microscopically on Loeffler's medium. After one week's incubation, anaerobically, coccoid and bacillary forms were found, and also long, irregular organisms varying from 0.5 to 1.5 microns in width and up to 10 microns in length (fig. 8). These showed considerable variation in shape; they stained either diffusely

Fig. 10.—Same as in figure 9, but this culture showed an unusual number of bottle-shaped bacilli. × 1,100.

or irregularly, and branching was observed frequently. Plasma cell forms were not present.

With aerobic cultivation on 1 per cent dextrose agar slants, irregularity in staining is not as marked as in anaerobic cultivation, whereas irregularities in morphology are greater (figs. 9 and 10). Coccoid forms and short and long bacillary forms up to 4 or 5 microns in length are present. Dumb-bell, oat, wedge, bottle and club shapes occur along with those having a more regular contour. Although the size of the organism varies considerably, it is on the whole larger than when cultivated anaerobically. In some instances suggestive branching is observed, but it is not as marked as on Loeffler's medium. A few of the plasma cell forms are occasionally encountered, but these are comparatively rare, and a diffuse staining of the cell is the rule.

Spore formation or the presence of a capsule could not be demonstrated.

COMPARISON OF ACNE BACILLUS A WITH ACNE BACILLUS B

A. *Cultural.*—A marked difference exists between the rapidity of development of the two varieties. This occurs on all the different mediums used, but is especially striking in deep shake tubes. When grown in this manner the colonies of acne *B* are well developed in four or five days, while those of acne *A* are only the size of a pin point or slightly larger. In thickly seeded tubes acne *A* grows with a characteristic zoning which has never occurred with any of the strains of the *B* variety that have been studied.

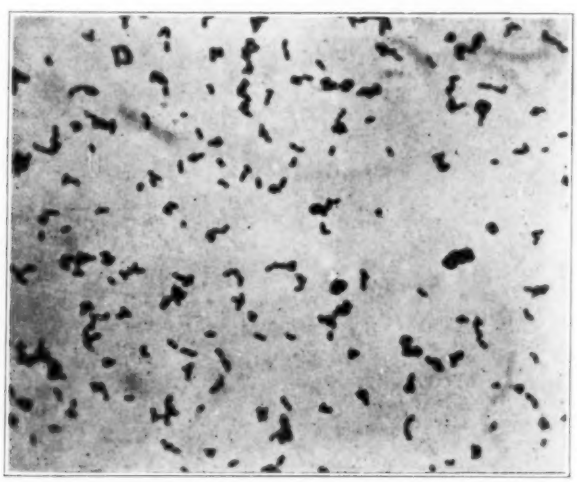

Fig. 11.—Acne bacillus *A* after two days' anaerobic cultivation on 1 per cent dextrose agar. × 1,100.

On solid mediums the greatest difference between the two varieties occurs when they are grown anaerobically on 1 per cent dextrose agar. At first, definite distinction is not apparent, but as the cultures grow older, acne *B* gradually assumes a dry appearance, a metallic luster and often a thin scalloped edge. The *A* variety always remains moist in appearance, even after two or three months' time, and is never crumbly when broken up with the platinum needle.

The most striking variations between the fermentation reactions of the two groups were that adonitol, sorbitol and lactose were fermented by a majority of the acne *A* strains and by none of the acne *B* strains. On the other hand, all of the acne *B* strains fermented maltose and one half of them raffinose, whereas these substances were attacked

by the *A* variety in only one instance. A slight tendency to ferment dextrin and starch was also shown by the former and not by the latter.

Acne *B*, on solid mediums at room temperature, remains viable for about four weeks, but the *A* variety will live for two months or longer under similar conditions.

B. *Morphologic.*—For the purpose of comparison four strains of acne *A* were studied with the *B* strains. In anaerobic cultures the acne bacillus *A* appears usually as a rather short plump organism, from 6 to 8 microns by 1.5 to 2 microns, although thinner forms may occur (fig. 11). The ends are round, and the bacillus is frequently slightly curved. It occurs singly or in short chains or clumps, and diplobacillary forms are common. Coccoid forms and irregular shapes

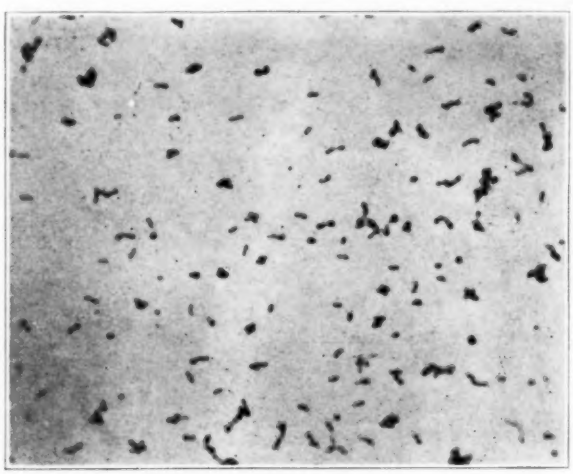

Fig. 12.—Acne bacillus *A* after six weeks' anaerobic cultivation on 1 per cent dextrose agar. × 1,100.

are also encountered. In older cultures (four or five weeks) the bacillus often becomes somewhat attenuated and irregular; longer forms occur with some irregularity in staining occasionally, but the plasma cell types characteristic of acne *B* have not been encountered (fig. 12). Aerobically, the acne *A* organism is more irregular than when grown anaerobically, but definite branching forms have not been seen (fig. 13). In some cultures two or more months old, most of the organisms were coccoid, varying a great deal in size and shape.

In broth cultures both coccoid and bacillary forms occur. Chains and clumps are seen frequently which are indistinguishable from those of streptococci (fig. 14).

The most marked variation between the two varieties occurs in anaerobic cultures on 1 per cent dextrose agar. On this medium the

B organism assumes, after one or two weeks' time, characteristic involution forms which have not been found in acne *A*, although in very young cultures no essential difference between the two may be observed. When cultivated aerobically on the same medium the differ-

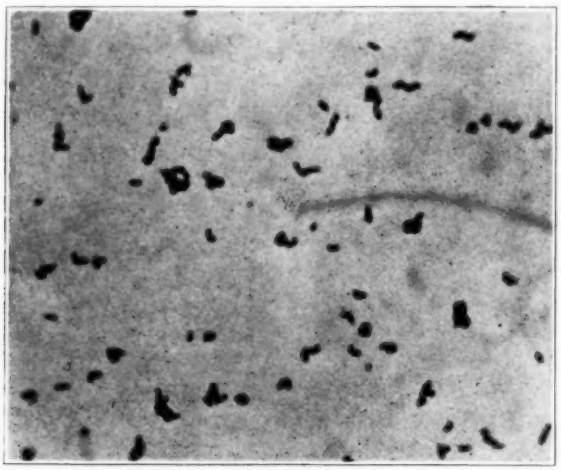

Fig. 13.—Acne *A*, 2 weeks old aerobic culture on 1 per cent dextrose agar. × 1,100.

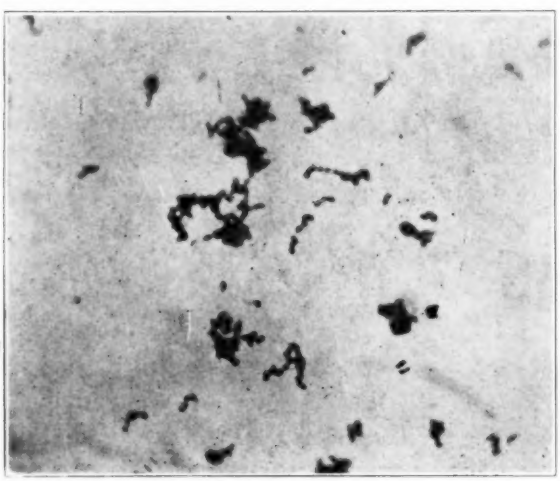

Fig. 14.—Acne *A*, 10 day old broth culture. × 1,100.

ence is not so marked, since under these conditions acne *B* does not show to any extent the characteristic plasma cell forms which develop with anaerobic cultivation. Larger involution forms, however, are seen in the *B* than in the *A* variety when grown in this manner.

COMMENT

Since acne *B* is much less frequently found than acne *A*, which is constantly present in all seborrheic filaments and acne lesions, the latter variety is believed to be the one which has been studied by most previous investigators. The *B* variety, however, must have been present occasionally in the cultures of those who have transplanted portions of filaments or acne material on to agar slants to isolate the organism.

Among those who have obtained the acne bacillus from deep shake tubes, Molesworth [3] alone mentions the development of red colonies in his tubes which were larger than the grayish white ones of the acne bacillus. He states that these were coccobacillary forms unlike the plump bacilli of acne, but further mention of the organism was not made.

The fermentation reactions recorded above, as well as those of other investigators, show considerable variation in these organisms. Südmersen and Thompson,[4] working with two strains of supposed acne bacilli, found that both fermented inulin and arabinose, neither of which were fermented by any of the strains herein recorded. Eberson [5] states that several strains which he has studied did not form acid in raffinose or dextrin. This observation, as far as it goes, corresponds with the results in my acne *A* strains.

CONCLUSIONS

1. A bacillus with cultural requirements and distribution, on the skin, similar to the acne bacillus is described.

2. Because of this general similarity it is regarded as a variety of the acne bacillus and designated acne bacillus *B*. The usual form is referred to as acne bacillus *A*.

3. The *B* variety differs from the *A* variety principally in its more rapid growth, the absence of zoning in deep shake tubes and the occurrence of certain characteristic involution forms in anaerobic cultivation. Other differences in the appearance of the growth of the two varieties and in the fermentation reactions are described.

DISCUSSION

Dr. George D. Culver, San Francisco: Formerly I was greatly interested in growing the acne bacillus, but did not succeed in getting such excellent growths as those of Dr. Ketron. He deserves credit for bringing this before the association.

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3. Molesworth: Brit. M. J. **1**:1927, 1910.
4. Südmersen and Thompson: J. Path. & Bact. **14**:224, 1910.
5. Eberson: J. Infect. Dis. **23**:1, 1918.

DR. JAY FRANK SCHAMBERG, Philadelphia: I would like to inquire whether the so-called acne bacillus cannot be cultivated from the sebaceous filaments expressed from the skin of the nose, even in persons who do not have acne.

DR. LLOYD W. KETRON, Baltimore: In answer to Dr. Schamberg's question, the organism was found in seborrhea without acne as well as in seborrhea with acne. The acne bacillus may be found in any one's nose if sebaceous material is present.

A CASE OF POIKILODERMA ATROPHICANS VASCULARE

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AND

ERIC C. CLARK, M.D.

BOSTON

Poikiloderma atrophicans vasculare is such a rare and unfamiliar disease that the report of an additional case seems to be warranted. In the literature eighteen certain cases and four doubtful cases are recorded. The first fourteen cases have been summarized by Lane.[1] Four other cases have been reported since, one by Capelli [2] in 1922, one by Wertheimer [3] in 1922, one by Rasch [4] in 1925, and one by Louste, Thibaut and Cailliau [5] in 1925. The reports of these four additional cases yield nothing new concerning the etiology, symptomatology or treatment of the disorder. In general, the disease appears to have varying symptoms which have a marked resemblance to healed roentgen-ray dermatitis. It appears to be entirely of unknown etiology.

For further descriptions of the condition and the views of the various dermatologists, the reader is again referred to Lane's [1] article in which there is an excellent summary of these facts.

REPORT OF A CASE

History.—The patient was a white man, aged 39, married, with one living child. The grandparents and parents on both sides were born in Sweden. The father was killed accidentally at the age of 54. The mother was living and well at the age of 67 and had never been sick. There were two brothers and three sisters living and well. One brother and one sister died of influenza in 1918. There was not a history of skin disease, tuberculosis, cancer or mental or nervous disease in any member of the family.

The patient was born in Stockholm, Sweden, Feb. 11, 1889. He was one of twins, the other twin being a sister who was strong and healthy, and who had

1. Lane, J. E.: Poikiloderma Atrophicans Vasculare, Arch. Dermat. & Syph. **4**:563 (Nov.) 1921.

2. Capelli, J.: Poikilodermia Atrophicans Vascularis "Jacobi," Gior. ital. d. mal. ven. **63**:617, 1922.

3. Wertheimer, H. G.: Poikiloderma Vascularis Atrophicans, Arch Dermat. & Syph. **6**:252 (Aug.) 1922.

4. Rasch, C.: Poikiloderma Atrophicans Vasculare, Brit. J. Dermat. **37**:477 (Nov.) 1925.

5. Louste, Thibaut and Cailliau: Bull. Soc. franç. de dermat. et syph. **32**: 48 and 114, 1925.

never been sick. The patient was weak from birth, and was always regarded as being somewhat sickly. He was slow in learning to walk and talk. He had measles, whooping cough and other sicknesses of childhood, which are not definitely known. It was said that he had a "weak stomach" from infancy and his diet had always been carefully watched. He started to go to school at the age of 5, and attended until he was 16. His attendance was irregular. The patient said that it was because of stomach trouble. He also said that he could not learn his lessons well, and that the teachers often cuffed his ears because he was stupid. He never took much interest in sports or games. He started to work on leaving school, in 1903, when he was 16 years old. He worked at numerous occupations, but principally as a carpenter or as a farm hand. From 1913 to 1917, he roamed about the world, and an adequate account of his wanderings has never been obtained. From 1917 until the summer of 1924, he worked as superintendent of a Salvation Army hotel. He left at that time because of ill health and had not worked since. His habits, as far as known, were always moderate. He took an occasional drink of alcohol, but the drinking was never excessive. He smoked moderately. He never used drugs. He was married in 1910, when 23 years old, and had one daughter, 14 years old, who was in good health. He left his wife after one year, because she accused him of infidelity. He had not had any sexual experiences outside of marriage, as far as was known.

In the winter of 1910, when the patient was 23 years old, both hands and both feet were frost-bitten. As a result he lost a part of his right thumb. After that his hands were always blue or white during the winter, and he suffered extremely from the cold. His brother said that shortly after this a slight rash appeared on his face. The rash was present only when the patient was warm, and then it resembled "pale pink blotches." In 1915, the patient was operated on at the Newton Hospital for an infected thumb, and the terminal phalanx of the thumb was removed under ether. The wound healed well, and the patient was then discharged. On Aug. 17, 1917, the patient was examined by Dr. George L. West and Dr. Edward A. Andrews of Newton for admission to the army under the draft. At that time it was noted that the ends of the thumb and first and second fingers of the right hand were missing, that he was weak and that there was an eruption over the body. There were varicose veins on the right leg. The nose was pinched, and there was partial obstruction on both sides. The heart and lungs were normal, and the vision was 20/20 in each eye. He had numerous carious teeth, and many teeth were missing. The history of the patient's condition from 1917 to 1923 was not available. The brother said that during the summer of 1923 the spots had become more noticeable on the face, body and extremities. In May, 1924, the condition of the skin became worse. The spots on the forehead became prominent and spread over the body. They were small at first and spread in patches. They were a pale red, but when the patient became cold the spots would turn blue. He suffered greatly from the cold. Even on hot days he would complain of feeling chilly. The skin did not cause discomfort at any time. Most of the time he did not have any abnormal sensation, but occasionally he would say that the eruption itched a little. In June, 1924, the ring finger of the right hand gradually became black, starting at the tip and extending down to the second phalangeal joint, gradually drying up. The patient tied a string around the finger "to help nature along." In about two weeks the finger had completely dried up. The patient then took a safety razor blade and cut it off. While the gangrene was progressing, the patient did not feel pain and amputation of the finger was

not painful. The wound healed rapidly in from three to six days and it was dressed with carbolated petrolatum. In July, 1924, the great toe of the left foot became gangrenous down to the metatarsal phalangeal joint. Gangrene took place as in the finger noted previously. About the end of August, 1924, the great toe of the right foot underwent a similar change, and in October, 1924, the second toe of the left foot was affected in the same way. Six weeks later the second toe of the right foot went through the same process. About this time he developed what was probably an acute cellulitis, which first extended up the right foot to the right knee and later behaved in a similar way on the left side. Further details concerning this were lacking. Some time during the winter or spring of 1925, the right arm became edematous. There was apparently an acute inflammation, and after one or two weeks the swelling subsided, leaving the fingers of the right hand atrophied and stiff. Before the condition in the right arm had completely cleared up, a similar change occurred in the left arm, so that for some weeks the patient had to be fed and could use neither hand. The fingers of both hands were atrophied and stiff from that time on. The patient's condition remained unchanged through the summer and fall of 1925. In December, 1925, he seemed to be failing rapidly. A slight difficulty in swallowing, which had been present for nearly two years, became markedly increased. "It seemed as though something was holding my gullet, at the entrance of the stomach. I could eat things that were ice cold. I used to drink gallons of water and milk and anything of the like, provided it was cold. Anything hot disagreed with me, and I would soon vomit it. I think it must have been some sort of a growth." From that time the patient became progressively worse. He had frequent attacks of vomiting. He said that about March 1, 1926, he felt something wriggling in his throat. He finally coughed up something which he thought was a tapeworm. In December, 1925, the patient became suspicious, and expressed the idea that his mother was trying to poison him by putting carbolated petrolatum and drugs in his food. He grew childish. He had frequent spells of depression and would often cry. At other times he would become extremely angry at his mother and sisters. He would yell and curse at them, but whenever his brother or strangers came in he would behave in a normal way. On March 20, 1926, he was admitted to the Roxbury Hospital. He was transferred from there to the Boston Psychopathic Hospital on March 29, because it was felt that he showed sufficient mental symptoms to warrant the diagnosis of a psychosis of an obscure nature.

When admitted to the Boston Psychopathic Hospital the patient was cheerful, cooperative and childlike in his attitude and behavior. His intellectual functions appeared to be intact without any evidence of hallucinations or delusions.

Physical Examination.—The patient was 5 feet, 4 inches tall and weighed 86¾ pounds (39.3 Kg.). He was greatly emaciated. The cheeks were sunken, there was shrinking of the tissues of the nose, the lobes of the ears were shrunken and the hair was long, dry and fine. The eyes were prominent and fixed, and there was a cataract in each. The teeth were all out. They were removed two years before as a possible source of infection. The chest was normal in size and the abdomen protuberant. This, combined with the atrophy of the muscles of the shoulder girdle, gave the body a bizarre appearance, as if the shoulders were much narrower than the hips, in transverse measurements. The supraspinatus and infraspinatus and the pectoralis muscles, in fact, all the muscles of the shoulder girdle and arm, were wasted. The fingers of the left hand were atrophied. The joints were all stiff, with limited movement. There was a

moderate degree of contracture, so that the fingers were partially flexed and drawn out of line. On the right hand the thumb was missing from the last interphalangeal joint, with a partial nail formation, a result of frostbite in 1910. The ring finger was missing from the second phalangeal joint, as a result of the gangrenous process of June, 1924. The other fingers were atrophied and flexed, owing to the contraction of the flexors. The pubic distribution of

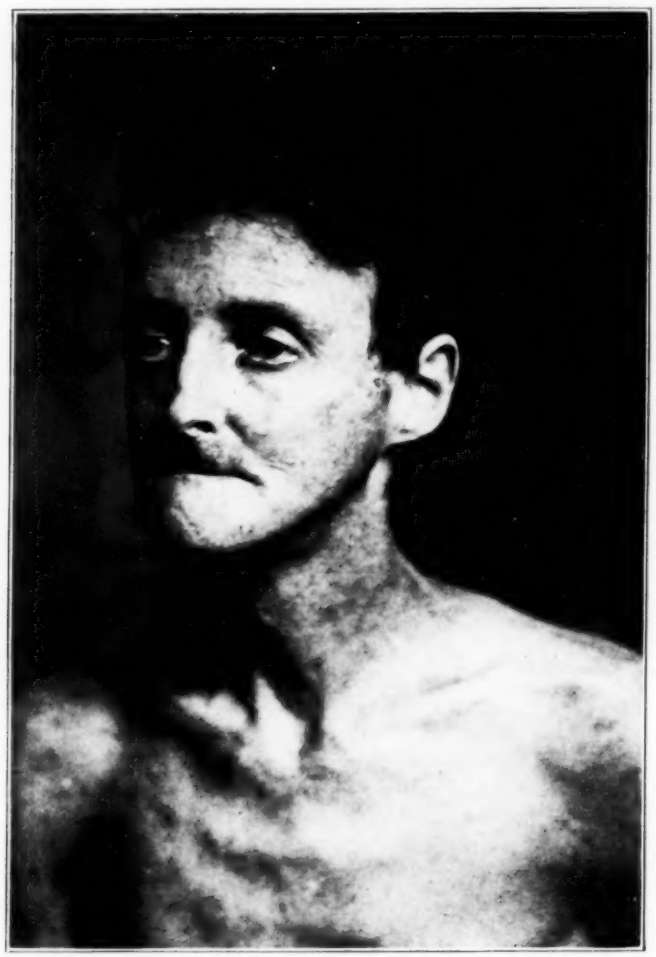

Fig. 1.—Showing distribution of lesions on face, neck and upper thorax as well as atrophy of nose and ear lobes.

hair was distinctly feminine; it was scanty and of fine texture. The penis was poorly developed and the scrotum pendulous. Both lower extremities showed marked atrophy of muscles. The first, second and third toes on the left foot were missing as a result of the gangrenous process of 1924 and 1925. There was a limitation of movement of the ankle joint. The second and third toes on the right foot were missing. The skin was dry and brittle. On the right

elbow, the right knee and both ankles were shallow ulcers with a slightly raised margin and an unhealthy surface, discharging a small amount of pus. The area surrounding the ulcers was plum-colored. The skin of both legs was thickened and discolored a bluish brown which the patient said was a result of the old cellulitis. On the face and neck there were areas, irregular in shape and size, varying from 0.5 cm. up to one large patch across the forehead, 4 cm. long by 2.5 cm. at the widest point and 1 cm. at the narrowest. A second large patch below the left eye, extending over the cheek and up to the midline over the nose, measured 4.5 cm. by 2.5 cm. The spots were smaller and paler on the lower part of the face, where there was a growth of hair. The scalp was

Fig. 2.—Showing distribution of lesions on forearm and hands as well as atrophy, contracture and missing parts of thumb and fingers.

free from spots. These spots were plum-colored, with fine capillaries in them. They were in the tissues, not raised above the surface. The skin over them was sensitive, but not more so than the surrounding tissue. They were not itchy or sore and never had been, according to the patient. Over the back there was an irregular distribution of patches of varied size, more diffuse and irregular than on the face. These patches were longer, narrower and more irregular in shape, and tended to coalesce. The chest and abdomen showed occasional spots, smaller, paler and isolated, with less tendency to coalesce. The lesions on the arms showed the same distribution, on both the flexor and extensor surfaces. The patches were smaller, mostly isolated, and extended down on to the back of hands. The palms showed a few small pale areas. The

lower limbs showed the patches down to the knee, but these patches also were pale and diffuse, with a slight tendency to coalesce. Below the knees the cellulitis had changed the skin, and while there was an occasional patch on the calf of each leg, the anterior surface was free from them. There were a few patches on the roof of the mouth and on the mucous membrane of the cheeks of the same type as those on the skin, but they were pale and small, with little tendency to coalesce.

Fig. 3.—Showing thickened, bluish brown skin, atrophy and missing parts of toes.

The heart and lungs were normal. The blood pressure was 132 systolic; 88 diastolic. There was some dulness in the flanks when the patient was lying on his back. The dulness shifted when he turned on his side, and it was thought to be caused by fluid. Masses were not felt. The spleen was not palpable. The margin of the liver was normal. The inguinal glands were enlarged and hard, about the size of a bean.

The neurologic examination showed that the pupils were fixed and did not react either to light or in accommodation. There was a cataract in each eye, said to have developed during the previous six months. Vision was impaired. The reflexes were normal, but those of the knees and ankles could not be obtained because of numerous ulcers on the knees and ankles. Results of the neurologic examination were otherwise negative.

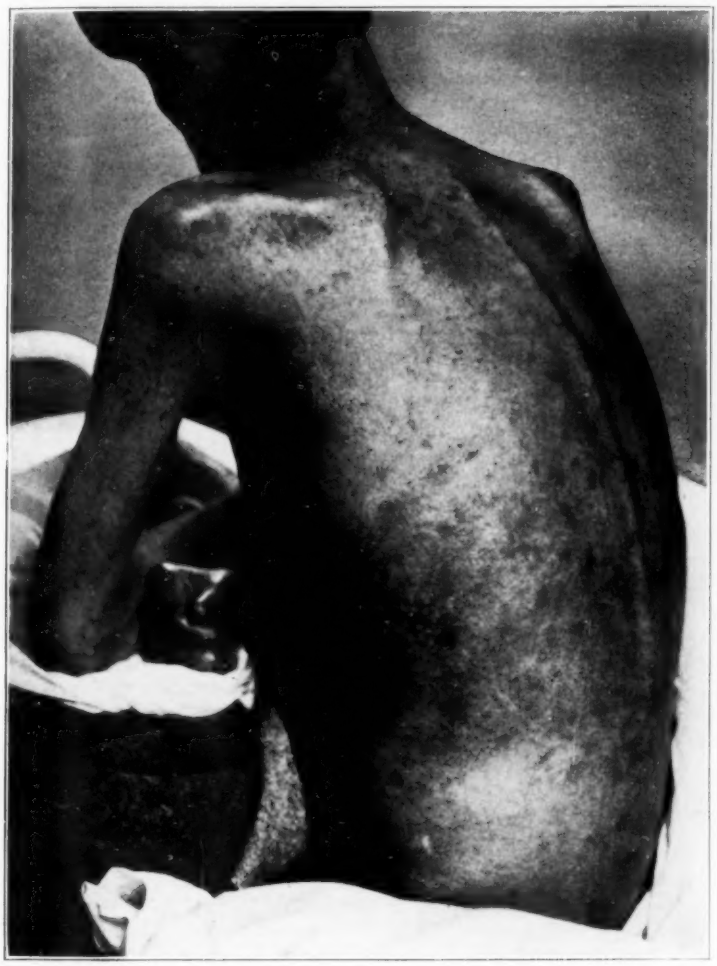

Fig. 4.—Showing irregular and more diffuse distribution of lesions on the back.

Laboratory Examination.—When the patient was admitted to the hospital, the urine was straw-colored and cloudy; the specific gravity was 1.014; the reaction was acid; there was a slight trace of albumin. Tests for sugar and bile were negative. The microscopic examination showed occasional hyaline casts, cylindroids, mucous shreds and from four to six white blood cells per

high power field. Results of later examinations of the urine were completely negative. The blood count on admission was as follows: hemoglobin, 70 per cent; red blood count, 4,630,000; white blood count, 16,100. A white blood count taken five days later was 9,800, and a differential count showed 51 per cent polymorphonuclear leukocytes; 5 per cent eosinophils; 1 per cent basophils; 36 per cent small lymphocytes, and 5 per cent large lymphocytes. Examination of the stool showed that it was formed and soft, without parasites or ova. The stool was a peculiar light yellow, with a light yellowish sheen. The benzidine test for occult blood was positive. An examination of the cerebrospinal fluid gave the following results: the fluid was clear, the cell count three, consisting of two small lymphocytes and one large lymphocyte. The result of the globulin test was 2 plus; total protein 91, sugar 79; the colloidal gold reaction was negative. The result of the Wassermann test was negative on the blood and on the spinal fluid. A chemical analysis of the blood showed: nonprotein nitrogen, 35; creatinine, 1.3; uric acid, 4; amino-acid, 5.2; calcium 10.8; chlorides, 618; sugar, 92. The basal metabolism rate was —15½ and —14, the second test being made twelve days after the first. The blood sugar curve showed the fasting blood sugar to be 87 mg. per hundred cubic centimeters. One hour after the ingestion of glucose, it was 115; at the end of two hours, it was 112; and at the end of three hours, it was 77. The nasal smear did not show acid-fast bacilli. Several blood cultures were taken, two of which were apparently positive, but the death of the patient prevented further studies, and the organism was not identified.

Roentgen-Ray Examination.—Dr. Whitman K. Coffin. There was considerable atrophy of the phalanges, the metacarpal and metatarsal bones; also of the ends of the radii, the ulnae and the tarsal bones. The surfaces of several of the phalangeal joints were apparently destroyed and several phalanges were missing from the hands and feet. Results of examination of knees and sinuses and of the skull were negative. The sella was rather small, but otherwise normal. The heart was large, but not distinctly above the normal limit of size. The lungs showed considerable peribronchial thickening, more marked in the bases than elsewhere. Definite evidence of tuberculosis was not present. The gastro-intestinal series showed that the stomach was small, hypertonic and high in the abdomen. The duodenal bulb was distorted because of the high position of the stomach. A definite defect in filling of the stomach or cap was not noted. The duodenum, however, was dilated and evidently obstructed about the point of junction with the jejunum, perhaps actually in the jejunum. The distal half of the duodenum (third and fourth portions) was distended and filled with solid matter, rather than the normal flaky content of the barium meal. The observations suggested adhesions, ulceration or neoplasm, the first being more likely, as the defects in filling characteristic of the last two were lacking. A second gastro-intestinal series showed possible gastric and duodenal abnormality, but the patient refused to drink the entire meal, and became sick before all the pictures could be taken.

Diagnosis.—On March 31, the patient was seen by Dr. George C. Shattuck, who felt that Raynaud's disease might account for the condition of the hands and feet, but that it did not explain the rash. He suggested that lathyrism and ergot poisoning should be considered, but felt they were unlikely. He felt that leprosy could be definitely excluded. He also suggested than an examination for carcinoma of the rectum be made, as there was some fluid in the abdomen.

On April 1, the patient was seen by Dr. Charles J. White, who suggested four possibilities: leprosy, syringomyelia, Raynaud's disease and poikiloderma atrophicans vasculare. Dr. White felt that the first three conditions could be ruled out, as the picture and clinical observations were not completely consistent with any one of these diseases. He felt that the condition of the skin could be definitely diagnosed as poikiloderma atrophicans vasculare.

Course.—During his first two weeks in the hospital the patient improved physically. The evidence of fluid in the abdomen disappeared. The condition of the skin remained unchanged. On April 28, one month after admission, a gastro-intestinal roentgen-ray examination was made. As the elevator was being repaired, it was necessary for the patient to walk down two flights of stairs. On his return, he was exhausted and felt chilly. His temperature rose to 102 F., his pulse rate became rapid, and he felt depressed. For several days he felt sick and weak. He had cramplike pains in the abdomen, was nauseated and vomited mucus. His temperature was slightly elevated. There was no abnormal rigidity or tenderness. The colored areas of skin on the forehead were a little paler than when the patient was first admitted. The patient's white blood count was 18,000. On April 30, the temperature returned to normal. He appeared even more cheerful than usual, and said that he felt splendid. His appetite was much improved, and diarrhea, which had been present for a short period, had entirely stopped. There was a slight frontal headache, but otherwise he did not complain. He gained slowly, and on May 3 he was allowed to sit up in a chair for a few hours. He continued improving until May 10. About noon of that day he complained of weakness, nausea and diarrhea. His temperature rose to 104 F., and he appeared acutely ill, although further signs could not be made out. The next day his temperature was again 104 F. The white blood count was 36,300. His temperature gradually subsided, and he improved. On May 17, he was discharged to the City Hospital, as evidence of psychosis had not been obtained during his stay in the hospital, and he insisted on leaving. On the day of discharge his temperature was 101 F. Otherwise, his condition was not changed.

After he was admitted to the Boston City Hospital, the patient complained of increasing weakness and stiffness of the arms and legs. The physical examination did not show further results than those previously reported. It was felt that, since the loss of eyesight bothered the patient most, this should be attended to before any considerations as to the value of organotherapy or other means of treatment. He was accordingly transferred to the eye service, and the cataract was removed from the left eye. During his convalescence from this operation the patient suddenly developed acute signs of cardiac decompensation, which were dyspnea, orthopnea, cyanosis and ascites. He died on July 25, 1926. It was thought at the City Hospital that the picture was that of an advanced scleroderma with atrophy of the muscles.

Autopsy.—Autopsy was performed sixteen hours post mortem by Dr. C. L. Swan, Jr.

The body was that of a well developed, poorly nourished white man. Rigor mortis was complete. There was a slight lividity of the back. The pupils were unequal; the right was 3 mm. in diameter; the left 5 mm. There was a double cataract. Edema was not present. A blotchy purplish macular rash was present over the face, back, sides and extremities. The macules varied in size from 2 mm. to 1 cm. Several ulcers were found on the bony prominences of the lower extremities; the largest, measuring 2.5 by 1.5 mm., was on the internal malleolus of the right foot. Areas of scar tissue with brownish pig-

mentation existed over the shafts of the lower extremities. The skin appeared smooth, shiny and atrophic, particularly over the nose and hands. Both hands were atrophic and contracted; the distal phalanx of the thumb of the left hand and the distal phalanx of the ring finger of the right hand were missing. The terminal phalanges of the first and second toes of the left foot and of the second toe of the right foot were absent. There were no palpable superficial lymph nodes.

In the peritoneal cavity the surfaces were smooth and glistening, and it contained 2,000 cc. of clear, straw-colored fluid. The appendix was normal and was 7 cm. long. The mesenteric lymph nodes were slightly enlarged, but soft. The dome of the diaphragm was at the level of the left fifth rib and the right fourth space. The edge of the liver was 2 cm. above the xiphoid, and 1.5 cm. above the costal margin in the right midclavicular line.

Firm fibrous adhesions were found at the base of the right lung, and a few fibrous adhesions over the anterior surface of the upper lobe of the left lung. The remaining surfaces were smooth and glistening, and there was about 250 cc. of clear, straw-colored fluid in each pleural cavity.

The surfaces in the pericardial cavity were glued together by fine fibrous adhesions. It did not contain free fluid.

The heart weighed 440 Gm. The epicardium was dull gray and rough (see description of pericardial cavity). The myocardium was pale grayish brown and somewhat soft, showing a grayish white streaking of fibrosis. The endocardium and the valves were normal. The coronaries showed moderate sclerosis. The measurements were: tricuspid valve, 11 cm.; pulmonary valve, 8 cm.; mitral valve, 10 cm.; aortic valve, 6.5 cm.; left ventricle, 1 cm., and right ventricle, 0.4 cm.

The lungs were a dark grayish blue, soft, elastic and crepitant. The cut surface was dark reddish gray, and a frothy serous fluid oozed from it on pressure. The bronchi were normal.

The spleen weighed 150 Gm. The surface was smooth and grayish purple; a cut section was dark red. The pulp was moderately firm and the gastrointestinal tract was normal. The pancreas was normal.

The liver weighed 1,418 Gm. The surface was smooth and dark grayish brown. The cut surface was dark brown with distinct yellow mottling. The gallbladder and ducts were normal.

The kidneys were of normal shape, but were unequal in size; the left weighed 200 Gm., the right, 115 Gm. The capsules were easily stripped off, leaving a smooth granular, pale brown surface. The cut surfaces were brownish red, with distinct markings. The cortices measured 0.5 cm. in thickness. The pelvis and ureters were normal, as were the suprarenal glands, the bladder and the genital organs.

The thoracic portion of the aorta was smooth, with noticeable longitudinal and a few stellate striations. The abdominal portion was roughened, with raised calcified yellow plaques, some of which showed ulceration.

The thyroid gland was of normal size and moderately firm. The cut surface was a pale pinkish brown. The head was covered with short, dark brown hair. The scalp was clean, and the calvarium was normal. The brain weighed 1,410 Gm. The leptomeninges were normal. The brain was firm and was pinkish gray. Edema was not present nor was there any abnormal injection of the vessels. The convolutions and the sulci were normal. Multiple sections did not reveal a pathologic condition. The pituitary gland, the middle ears and the spinal cord were normal.

Anatomic Diagnosis.—The dermatologic diagnosis was poikiloderma vascularis atrophicans, including: (*a*) cutaneous macular rash, (*b*) "trophic" ulcers, (*c*) atrophic contracture of the hands and (*d*) absence of the terminal phalanges of the fingers and toes. There were also chronic vascular myocarditis, fibrinous pericarditis, old pleuritis and double hydrothorax, chronic passive congestion of the liver, ascites and arteriosclerosis.

Microscopic Examination (Dr. F. B. Mallory).—The epicardial surface of the heart showed fibrous thickening, with moderately diffuse infiltration with lymphocytes and occasional endothelial leukocytes. Throughout the myocardium there were focal accumulations of lymphocytes, with occasional eosinophilic and neutrophilic polymorphonuclear leukocytes. About these areas the muscle fibers were thinned out and showed some hyaline change. There was moderate sclerosis. The blood vessels were congested, and the stroma was edematous.

Numerous foci of lymphocytes were found along the pleural surface of the lungs. The alveoli were filled with granular precipitate and pigmented endothelial leukocytes. A section from the firmer portion of the lung showed marked fibrosis; the alveolar walls were thickened, and the alveolar spaces, to a great extent, were filled with granulation tissue. Other alveoli were filled with red blood cells, endothelial leukocytes and foreign body giant cells surrounding cholesterin crystals. There was a moderate degree of carbon pigment.

There was hyaline thickening of the intima of the blood vessels of the spleen. The pulp was moderately infiltrated with polymorphonuclear leukocytes and there was a slight increase in stroma. The pancreas showed portmortem changes. A few scattered lymphocytes and endothelial leukocytes were found in connective tissue septums. The capsule of the liver was thickened. There was a margin of fibrosis with foci of lymphocytes beneath the capsule, and generalized hemorrhage and necrosis about the central veins. There were foci of lymphocytes about the periportal spaces. The kidneys contained occasional foci of lymphocytes and a few hyaline casts, but were otherwise normal, except for a slight congestion. In the suprarenal gland there was congestion with rare foci of lymphocytes. The testicle was normal.

There was a marked thickening of the intima in the aorta with necrosis, calcification and cholesterin crystals. Atrophy and disappearance of muscle fibers, numerous foci of lymphocytes and plasma cells were noticed in the media. The adventitia showed perivascular infiltration with lymphocytes. The thyroid gland was normal.

In the upper layer of the corium just beneath the epidermis there was an inflammatory exudate consisting of lymphocytes and endothelial leukocytes. The blood vessels were not unusual. Another section of skin showed an area of ulceration with inflammatory exudate, consisting chiefly of polymorphonuclear leukocytes. The adjacent blood vessels were undergoing necrosis. There was a fibroblastic proliferation around the edges of the ulcer. The upper layer of the corium away from the ulcer was edematous, and was infiltrated with lymphocytes, plasma cells and occasional polymorphonuclear leukocytes.

The bronchial lymph nodes were edematous and slightly congested. They contained many endothelial leukocytes, some with carbon pigment. There was slight edema of the pia-arachnoid and upper portion of the cortex; otherwise it was normal. The spinal cord was normal. A large focus of lymphocytes was found about the margin of the sympathetic ganglion. Within the ganglion there was a perivascular infiltration of lymphocytes and plasma cells. The cells of the ganglion were normal.

The microscopic diagnosis was chronic vascular myocarditis, sclerosis of the lung (probably following organization of a pneumonic exudate), chronic passive congestion and old hemorrhagic central necrosis of the liver, old perihepatitis and chronic inflammation of the sympathetic ganglion.

The following examination of the microscopic sections was made by Dr. Charles J. White.

Two sections were studied—one from an ulcer and one from the adjacent skin.

The ulcer presented nothing noteworthy. The epidermis was gone, and the corium was packed with inflammatory cells. Mononuclear elements, most of which were small, predominated. In addition, there were a few polymorphonuclear and still fewer plasma cells. Many newly formed vessels were present, and many young connective tissue cells which formed a delicate reticulum.

In the adjacent intact skin the epidermis was distinctly pathologic. The stratum germinativum appeared normal, but the overlying rete mucosum presented cells, throughout its depth, which showed marked perinuclear halos, and poorly staining cytoplasm. The nuclei, however, seemed to retain their vitality, if one can so interpret their sharp affinity for the dye. The rete as a whole was markedly acanthotic; the interpapillary pegs were deep and broad. The stratum granulosum was well marked—consistently with the degree of rete hypertrophy. The stratum corneum was decidedly abnormal. The cells were swollen, almost round. Parakeratosis was absent, but nuclear spaces seemed to persist uniformly, although their contents had invariably disappeared.

The corium seemed less affected than the epidermis. The papillae were universally long; some were broad as well. The constituting connective tissue was extremely delicate, as was that of the subpapillary layer. In these two layers the vessels were numerous, dilated and consequently conspicuous. Around the uppper horizontal layer of vessels there was a mild but obvious perivascular infiltration. The lower layers of the corium did not contain abnormalities.

Considering the pathologic condition of the skin as a whole, many variations from the normal were found, but there was nothing pathognomonic.

The following examination of the microscopic sections was made under Dr. Stanley Cobb's direction at the Department of Neuropathology, Harvard Medical School, by Dr. H. G. Wolff.

The general architecture of the suprarenal gland appeared normal, with the exception of a tear at one end. The staining was good. The cortical epithelium was normal in arrangement and character. The medulla contained many engorged capillaries and free red blood cells lying in the stroma (possibly post mortem). The walls of the blood vessels appeared normal. The sheath about the gland was somewhat thickened, with possibly a slight overgrowth of connective tissue. There were several small loci of round cell (leukocytic) infiltration. The medullary cells were for the most part normal in appearance, with the following outstanding exceptions: There were several areas of infiltration of lymphocytic red cells which, although for the most part in the medulla, extended also to the cortex. The red cells in the cortex were scattered, and were not as great as those in the medulla. There was no gross disorganization or degenerated tissue. The red cells were usually near a fair-sized blood vessel. There was not apparent overgrowth of connective tissue, although the cell structure underlying the masses of lymphocytes was not clear in most instances. In one place, however, it seemed as though the medullary cells were swollen, homogeneously stained, with a loss of finer cellular structures and eccentrically placed nuclei. The cells there appeared diseased.

The sympathetic ganglion was apparently normal in general architecture. There were no tears and the staining was good. The sheath or capsule was normal in appearance, except in one place in which there was a slight thickening and several small vessels with perivascular lymphocytic infiltrations. The ganglion itself, especially near the sheath, showed on one side a distinctly diseased process. There was some perivascular infiltration of round cells in this area and slight proliferation of connective tissue. The neurons of the ganglion were diseased, showing all stages of neuronophagia. In some of the cells little damage was apparent, but in others there were a loss of staining quality, a lack of differentiation in cell content, extruded nuclei and even rupture and disorganization of the wall of the cell. The cell was not engorged and the wall of the blood vessel was not thickened. Gross disorganization and degeneration were not present.

The structure of the cervical section of the spinal cord was apparently normal as to general cellular structure. The following abnormalities were observed: perivascular infiltration of round cells (lymphocytic) near the margin in the lateral-dorsal portion of the cord (white matter), and slight increase in the number of connective tissue and glia cells. The meninges were apparently normal as to blood vessels and cellular structure, with the exception of perivascular infiltration. Lateral horn cells were somewhat reduced in number; a few showed degenerative changes and some were pyknotic, but this was not a consistent nor marked condition. Neuronophagia was not noted. The ependymal canal was normal.

The thoracic section of the spinal cord was normal in appearance, with the following exceptions: There were occasional exaggeration of the perineural space and faint staining of cells in the dorsal lateral region of gray matter. Genuine neuronophagia was not present. The coating of the cord was normal. There was perivascular infiltration in vessels along the dorsal horn on the right. The roots were not diseased.

A section through the dorsal root (thoracic section) showed a slight lymphocytic perivascular infiltration. The cerebral cortex and the cerebellum were normal.

An examination of the cerebral cortex with the Morgan stain did not show evidence of bundle or tract degeneration. Throughout the tissues there were areas of colloid-like deposits, which were apparently artefacts. These did not play a constant rôle in the architectural make-up of the tissue. Disease of the bundle or tract was not noted.

The cerebellum, the basal ganglion, the hind portion of the hind brain, the lower cervical cord and the upper, middle and lower thoracic cord presented the same appearance as the cerebral cortex.

COMMENT

A study of the eighteen cases reported leads one to conclude that three possible causes of the disorder merit serious consideration: exposure, infection and endocrine disorder. The patients in the two cases reported by Zinsser [6] had frozen their fingers, and the early symptoms of the disease appeared in the hands. The case reported by Rasch [4] showed

6. Zinsser, F.: Atrophia Cutis Reticularis cum Pigmentatione, Dystrophia Unguium et Leukoplakia Oris (Poikilodermia Atrophicans Vascularis, Jacobi), Ikonographia Dermat. **5**:219, 1910.

that the condition had started on the patient's face after severe exposure to sunlight. The patient in the case reported in this article also showed his first symptoms shortly after having both hands and both feet frostbitten.

The question of infection, particularly of rheumatic origin, should be considered. Jacobi's [7] patient had been treated for pains in the joints for four years previous to the appearance of symptoms of the skin. Terebinsky's [8] patient had had pulmonary tuberculosis and malaria. Bruck's [9] patient had had a mild attack of rheumatism a few years before his symptoms appeared. Bettmann [10] said that his patient had suffered from cold and dampness for an entire winter five years preceding the onset of the condition. After this he had a furunculosis, and two years later muscular rheumatism. In Capelli's [2] case, the condition appeared in the patient twenty days after the birth of a child, so that infection might be considered, although positive evidence is lacking. In the case reported in this article the presence of positive blood cultures would likewise raise the question of an infectious origin of this disorder.

In the discussion of Lane's [1] article the question of an endocrine disturbance as the cause was raised by Dr. Sigmund Pollitzer of New York, who felt that "the entire picture of scleroderma and atrophoderma points doubtlessly to an endocrine disturbance." In the case reported here the low basal metabolism might be considered as evidence of an endocrine disorder. The microscopic examination of the thyroid showed essentially normal conditions. The suprarenal glands showed slight changes, and one might argue that suprarenal deficiency would cause a lower basal metabolism and might also produce the lesion of the skin, since it is known that in Addison's disease a change in the pigmentation of the skin occurs.

The fourth probability, which is not mentioned in the other cases reported, is that the condition may be of nervous origin. The definite observation of a distinct disease process in the sympathetic ganglions would indicate that the atrophic changes might be caused by lack of proper trophic stimuli from the sympathetic nervous system. It does not seem easy, however, to explain lesions of the skin on the same basis, although one might consider this possibility.

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7. Jacobi, E.: Fall für Diagnose (Poikilodermia Atrophicans Vascularis), Verhandl. d. deutsch. dermat. Gesells., IX Kongress, Bern **9**:321, 1907.

8. Terebinsky, V. I.: Poikilodermia Atrophicans Vascularis, Russk. Vrach. **15**:1057, 1916.

9. Bruck, C.: Ueber Poikilodermia Atrophicans Vascularis, Dermat. Wchnschr. **68**:369, 1919.

10. Bettmann: Ueber die Poikilodermia Atrophicans Vascularis, Arch. f. Dermat. u. Syph. **129**:101, 1921.

News and Comment

Externship in Dermatology and Syphilology Stanford University Medical School.—On Aug. 1, 1927, an appointment to this position will be made for the year 1927-1928. The salary will be $75 a month. About 300 syphilitic patients per week and an average of thirty dermatologic patients per day are treated. There are ample opportunities and facilities for research. Applications stating age and educational qualifications of candidate must be filed before June 1 with Harry E. Alderson, M.D., clinical professor of medicine (dermatology and syphilology), Stanford Medical School, San Francisco.

Death of Petrini-Galatz.—Petrini-Galatz, Roumania, former professor of dermatology, University of Bucharest, died recently.

Abstracts from Current Literature

TWO HUNDRED AND FORTY-THREE FETAL AUTOPSIES: A SYPHILITIC STUDY. J. R. MCCORD, J. A. M. A. **88**:626 (Feb. 26) 1927.

Only fifty babies of this series were born alive. The causes of death in the order of frequency were: syphilis, 57 per cent; brain hemorrhage and tentorial tears, 13 per cent; prematurity, 11 per cent, and toxemia of the mother, 4 per cent. McCord thinks that the bone lesion known as Wegner's disease is pathognomonic of fetal syphilis. Histologic study showed that the lungs, kidneys and liver were the tissues most frequently involved. Also *Spirochaeta pallida* was found most frequently in these organs in the order named. Negative observations of any kind cannot absolutely exclude syphilis.

SCARS: A NEW TRIPLE TECHNIC FOR REDUCING DISFIGURING CICATRICES TO A DEGREE OF INVISIBILITY AMOUNTING TO PRACTICAL REMOVAL. J. F. GRATTAN, J. A. M. A. **88**:638 (Feb. 26) 1927.

Grattan's technic is divided into three steps: (1) excision of the scar and linear approximation of the cut edges; (2) roentgen ray in a series of six treatments, and (3) leveling of any remaining elevations by cauterization with trichloracetic acid.

This technic has been used by the author in more than 1,000 cases in the course of seven years and the results have been satisfactory.

A TOXIC REACTION FROM PHENOBARBITAL (LUMINAL): REPORT OF SIX CASES. A. S. JACKSON, J. A. M. A. **88**:642 (Feb. 26) 1927.

Only seven cases of dermatitis medicamentosa produced by phenobarbital were found in the literature. Jackson's additional cases were all of a generalized erythematous maculopapular type, accompanied by intense itching, fever, vertigo, weakness and malaise. A patient should not be given this drug without warning of the possibility of a drug eruption resulting from its use.

MICHAEL, Houston, Texas.

THE TREATMENT OF LUPUS ERYTHEMATOSUS WITH NEOARSPHENAMINE: RESULTS: SPECIAL INTOLERANCE; SEROLOGY. PAUL RAVAUT and BOCAGE, Ann. de dermat. et syph. **7**:657 (Dec.) 1926.

Twenty-three cases of discoid lupus erythematosus were treated with neoarsphenamine. In one-third the lesions disappeared entirely, or almost entirely; in one-third there was a remarkable improvement; in the rest of the cases the treatment was abandoned because of intolerance, or because of ineffectiveness. In some instances it had to be prolonged before good results were obtained. One case also presented lesions of the diffuse variety, which disappeared readily under the injections.

These patients, in general, supported the drug badly, nausea and fever being the chief toxic signs. Conservatism in dosage was necessary.

In eight of the cases the Wassermann reaction was positive.

SEVEN CASES OF SUBACUTE INGUINAL LYMPHOGRANULOMATOSIS (NICOLAS AND FAVRE). P. GIACARDY, Ann. de dermat. et syph. **7**:675 (Dec.) 1926.

These cases are divided into three classes: In the first, the onset, following a trifling or even unnoticed genital lesion, is marked by indolent inguinal lymph node enlargement. In the second, the symptoms of onset are acutely inflammatory, as in chancroid, and in the third, the onset is accompanied by fever and signs of general infection.

SYPHILIS AND CHRONIC ASTHENIA. R. BENON, Ann. de dermat. et syph. **7**:686 (Dec.) 1926.

According to Benon, some cases of neurasthenia are of syphilitic origin and respond favorably to combined treatment with the arsenical drugs, mercury and bismuth, with or without potassium iodide. Cases of nonsyphilitic origin are often aggravated under such treatment. A therapeutic test lasting from three to six months is advised.

THE STRUCTURE OF THE SUDORIPAROUS GLANDS. A. BRANCA, Ann. de dermat. et syph. **8**:1 (Jan.) 1927.

In a well illustrated article, with a good bibliography, Branca describes in detail the cytology of the sweat apparatus, including the transition segment, found in the axilla, between the gland proper and the duct.

CONTRIBUTION TO THE ETIOLOGY OF THE JUXTA-ARTICULAR NODOSITIES OF JEANSELME AND LUTZ. I. OLESSOV, Ann. de dermat. et syph. **8**:22 (Jan.) 1927.

Three cases, in natives of central Russia, are reported, with photographs and photomicrographs. They were considered to be tubercular syphilides rather than gummas. Trauma may have had some part in their formation.

BISMUTH AND FUSO-SPIROCHETES. MANGABEIRA-ALBERNAZ, Ann. de dermat. et syph. **8**:34 (Jan.) 1927.

Local applications of a 10 per cent solution of the acid tartrobismuthate of potassium had a pronounced analgesic effect in Vincent's angina, in otitis due to the same organisms, and following the electric coagulation of tonsils. The applications are said to have been extremely effective in destroying the spirochete and the fusiform bacillus.

PITYRIASIS ROSEA (GIBERT) BEGINNING AROUND VACCINIAL PUSTULES. GOUGEROT and FILLIOL, Bull. Soc. franç. de dermat. et syph. **33**:688, 1926.

Two "herald plaques" of pityriasis rosea appeared at the site of a fresh vaccination; two weeks later there was a widespread eruption.

POSTTRAUMATIC SYPHILITIC GUMMA, FOLLOWING A DOG BITE. GOUGEROT and FILLIOL, Bull. Soc. franç. de dermat. et syph. **33**:688, 1926.

In a patient with syphilis of five years' duration, a gumma developed in a few days from a wound on the leg.

POSTTRAUMATIC GUMMATOUS SYPHILID FOLLOWING A SUBCUTANEOUS INJECTION OF CAFFEIN. GOUGEROT and FILLIOL, Bull. Soc. franç. de dermat. et syph. **33**:689, 1926.

The drug had been injected in the thigh, the gumma developing immediately afterward.

TREATMENT OF EARLY ARSENICAL REACTIONS WITH THE EOSINATE OF CESIUM. H. GOUGEROT and BERTILLON, Bull. Soc. franç. de dermat. et syph. **33**:691, 1926.

To prevent reactions, the arsphenamine is dissolved in from 5 to 10 cc. of a 5 to 6 per cent aqueous solution of pure and specially prepared cesium eosinate. Fever, vomiting and headache were thus prevented. The action of the eosinate in cases of erythroderma has not been tried.

POLYMORPHOUS TUBERCULIDS. SEZARY, NOVERO and LICHTWITZ, Bull. Soc. franç. de dermat. et syph. **33**:693, 1926.

Under observation for eight months, a woman, aged 39, presented disseminated nodular sarcoids, erythema induratum, granuloma annulare, papular tuberculids and papulonecrotic tuberculids. Axillary and tracheobronchial lymphadenopathy, apparently tuberculous, were also present.

BILATERAL SYPHILITIC DACRYOADENITIS. HUDELO, D'ALLAINES and RABUT, Bull. Soc. franç. de dermat. et syph. **33**:698, 1926.

In a boy, aged 13, whose infection was apparently congenital, the lacrymal glands of both eyes were involved. The condition subsided entirely under treatment with bismuth.

INTRANASAL SYPHILITIC CHANCRE. HUDELO, DUMET and FILHOULAND, Bull. Soc. franç. de dermat. et syph. **33**:701, 1926.

The right side of the nares was involved. The exact mode of infection was not determined.

GUMMATOUS TUBERCULOSIS OF THE UPPER EXTREMITY CURED BY CRYSALBINE (SANOCRYSINE). JEANSELME and BURNIER, Bull. Soc. franç. de dermat. et syph. **33**:703, 1926.

The thiosulphate of gold and sodium (crysalbine) was used, as in the treatment of lupus erythematosus. The lesion healed after the seventh injection.

SCLERODERMA IN PLAQUES WITH SYMMETRICAL PIGMENTARY DYSCHROMIA. JEANSELME and BURNIER, Bull. Soc. franç. de dermat. et syph. **33**:704, 1926.

In a girl, aged 18, brown patches were seen on the abdomen and back, of eight months' duration. Except in one area, the skin was of normal consistency. One patch, on the abdomen, showed the characteristics of scleroderma, and there were two other morpheic lesions.

CANCER OF THE TONGUE CURED BY RADIUM FOR THREE YEARS. E. WALLON, Bull. Soc. franç. de dermat. et syph. **33**:706, 1926.

Occurring in a girl, aged 21, the cancer was diagnosed histologically.

TREATMENT OF CERTAIN PRURITIDES IN WOMEN BY INJECTIONS OF ORCHITIC EXTRACT. JEAN MEYER AND GALLERAND, Bull. Soc. franç. de dermat. et syph. **33**:710, 1926.

Seven cases of rebellious pruritus cutaneous are reported, in elderly women, which were more or less completely benefited by injections of orchitic extract. Improvement usually followed the third or fourth injection.

A Case of Tabes Accompanied by Cutaneous and Mucous Lesions. Wahl, Bull. Soc. franç. de dermat. et syph. **33**:713, 1926.

In a man, aged 57, infected twenty-two years previously, there was a well developed tabes, and also tertiary syphilids of the scalp, legs, lips and tongue.

Malignant Pustule (Anthrax). L. Perin and Ricard, Bull. Soc. franç. de dermat. et syph. **33**:715, 1926.

In a girl, aged 18, engaged in the manufacture of bedding, a lesion was observed below the angle of the jaw. The local and general reactions were relatively slight, and recovery followed cauterization and six injections of anti-anthrax serum.

Syphilitic Mastitis. Delalande, Bull. Soc. franç. de dermat. et syph. **33**:717, 1926.

Bilateral tumors of six months' duration, in a girl, aged 21, infected in 1922, subsided after two injections of neoarsphenamine.

Trial of Quinosol in the Treatment of the Dermatophytoses. L. Lortat-Jacob and C. Bidault, Bull. Soc. franç. de dermat. et syph. **33**:719, 1926.

The introduction of quinosol into mediums prevented the growth of various vegetable parasites. The following preparations were used effectively against cutaneous lesions:

The solution:

Quinosol	0.5 to 1
Alcohol (90 per cent)	50
Glycerin	20
Boiled water	150

(Dissolve the quinosol in the water, and then add the alcohol and glycerin.)

The cream:

Quinosol	0.5
Boiled water	5
Lanolin	25
Petrolatum	70

Multiple Subcutaneous Lipomas in a Dahomian Soldier. A. Esquier, Bull. Soc. franç. de dermat. et syph. **33**:722, 1926.

The patient was a negro. His father was said to have had similar tumors.

Vegetating Pyoderma (Hallopeau). G. Milian, Bull. Soc. franç. de dermat. et syph. **33**:727, 1926.

This rebellious condition, in a man, aged 58, resembled pemphigus vegetans in its appearance and localization. Histologically, the lesions were perifollicular, and vesiculation was not present.

Traumatic Staphylococcic Pyoderma, Papillomatous and Verrucous. G. Milian and M. Kitchevatz, Bull. Soc. franç. de dermat. et syph. **33**:731, 1926.

In a carpenter, a vegetative patch resembling tuberculosis verrucosa cutis, appeared on the dorsum of the hand following an injury.

NITRITOID CRISES CURED BY MERCURY CYANIDE; INFECTIOUS URTICARIA. MILIAN and WAHL, Bull. Soc. franç. de dermat. et syph. **33**:733, 1926.

In a man with primary syphilis, a crisis following the first neoarsphenamine injection was treated with epinephrine hydrochloride intragluteally, and a painful local infection developed. Thirteen intravenous injections of mercury cyanide were given, and then neoarsphenamine was administered uneventfully. After the second arsenical injection, urticaria appeared, but failed to follow succeeding injections.

REMARKABLY EXTENSIVE TRICHOPHYTOSIS OF THE BUTTOCKS, DUE TO TRICHOPHYTON GYPSEUM GRANULOSUM. GEORGES LEVY and A. SLOIMOVICI, Bull. Soc. franç. de dermat. et syph. **33**:740, 1926.

In a child, aged 10, the deeply infiltrated lesions appeared rapidly. The source of infection was not determined.

MYCOSIS FUNGOIDES WITH TUMORS "D'EMBLEE." PAUTRIER and A. DISS, Bull. Soc. franç. de dermat. et syph. **33**:741, 1926.

In a butcher, aged 45, the condition was of two years' duration. Roentgen rays were used with benefit.

CIRCUMSCRIBED LYMPHANGIOMA OF THE BUTTOCK. J. ROEDERER, Bull. Soc. franç. de dermat. et syph. **33**:743, 1926.

Treatments with solid carbon dioxide and radium were proposed.

CONTINUOUS SUPPURATIVE ACRODERMATITIS (HALLOPEAU). R. GLASSER and A. DISS, Bull. Soc. franç. de dermat. et syph. **33**:744, 1926.

In a farmer, aged 69, the hands had been infected for twenty-five years. The histologic features are described.

TRANSITION FORM BETWEEN DERMATITIS HERPETIFORMIS, "HERPES GESTATIONIS" AND PEMPHIGUS VEGETANS. PAUTRIER and LANZENBERG, Bull. Soc. franç. de dermat. et syph. **33**:746, 1926.

This eruption, following childbirth, in a woman, aged 31, is minutely described, clinically and histologically.

INTERDIGITAL LESION OF BOTH HANDS, OF MYCOTIC APPEARANCE, PRESENT FIVE YEARS, ITS NATURE UNDETERMINED. GEORGES LEVY and A. SLOIMOVICI, Bull. Soc. franç. de dermat. et syph. **33**:757, 1926.

Occurring in a woman, aged 23, the eruption resembled the hyperkeratotic type of dermatophytosis; no organism was found.

SYPHILITIC REINFECTION AFTER EXTREMELY SHORT TREATMENT. GEORGES LEVY, Bull. Soc. franç. de dermat. et syph. **33**:759, 1926.

After less than a month of combined treatment for a proved initial lesion of the glans, the patient disappeared, with a weakly positive Wassermann reaction. Six and one-half months later he returned, presenting an apparently primary sore on the prepuce, with a negative Wassermann reaction. He had been exposed to infection two months previously.

VESICULOBULLOUS, PAPULAR AND TRANSIENT SUBCUTANEOUS NODULAR LESIONS, HISTOLOGICALLY APPROACHING MYCOSIS FUNGOIDES, IN A PATIENT WITH LYMPHOCYTOMA. PAUTRIER, A. DISS and LANZENBERG, Bull. Soc. franç. de dermat. et syph. **33**:763, 1926.

The eruption was widespread and of a month's duration, in a man, aged 46, who had noticed moderate lymph node enlargement for one and one-half years. The spleen was large. The leukocyte count was normal.

ACRODERMATITIS CHRONICA ATROPHICANS (HERXHEIMER-PICK), WITH TUMORS. P. MASSON and A. DISS, Bull. Soc. franç. de dermat. et syph. **33**:768, 1926.

The histologic report is given in detail.

AURICULAR AND PALPEBRAL XANTHOMA: ITS RELATIONS TO HYPERCHOLESTERINEMIA AND HYPERURICEMIA. SEZARY, LICHTWITZ and M. LEBLANC, Bull. Soc. franç. de dermat. et syph. **34**:7, 1927.

In a woman, aged 50, the eyelids had been involved for ten years and the ears for eight months. There was a slight hyperglycemia, and the blood cholesterin and uric acid were increased. Tophi may have acted as a foundation for the deposits in the ears.

DISSEMINATED SPOROTRICHOTIC ABSCESSES AND ULCERATIONS OF A LEG; ASSOCIATION OF THE SPOROTHRIX AND STAPHYLOCOCCUS AUREUS; PATHOGENESIS. SEZARY, COMBE and LICHTWITZ, Bull. Soc. franç. de dermat. et syph. **34**:11, 1927.

This condition, of one and one-half years' duration in a woman, aged 61, was diagnosed culturally. The exact manner of infection could not be determined.

FALSE TINEA, RETRO-AURICULAR IMPETIGO AND "SEBORRHEIDS." MILIAN and PERIN, Bull. Soc. franç. de dermat. et syph. **34**:16, 1927.

In a girl, aged 22, the same streptococcus was found in lesions of the scalp, ears and trunk.

LUPUS ERYTHEMATOSUS OF THE FACE IN A PATIENT WITH CONGENITAL SYPHILIS; CURE BY BISMUTH. LORTAT-JACOB and LEGRAIN, Bull. Soc. franç. de dermat. et syph. **34**:19, 1927.

A woman, aged 46, had discoid lupus erythematosus of six months' duration.

SOFT CHANCRE OF THE NECK OF THE UTERUS. LOUSTE, DUCOURTIOUS and LOTTE, Bull. Soc. franç. de dermat. et syph. **34**:20, 1927.

Inguinal lymphadenitis called attention to this chancroid.

OIL TUMOR OF THE BUTTOCK. HUDELO and RABUT, Bull. Soc. franç. de dermat. et syph. **34**:24, 1927.

A woman had received intragluteal injections nine years previously, but she had noticed the tumor for only five months. The contents were found to be oily.

A Case of Acute Lichen Planus in a Child. Lortat-Jacob and Robert Sicard, Bull. Soc. franç de dermat. et syph. **34**:26, 1927.

In a child, aged 8 years, the eruption was of abrupt onset, rapid evolution and generalized distribution. The buccal mucosa was not involved.

Two Cases of Zoster in Patients Receiving Bismuth. A. Galliot, Bull. Soc. franç. de dermat. et syph. **34**:27, 1927.

In the first case, the eruption appeared two months after a bismuth course had terminated; in the second, it followed the seventh injection.

Bismuth Abscess Due to Bismuth Carbonate. A. Galliot, Bull. Soc. franç. de dermat. et syph. **34**:29, 1927.

Developing four months after the end of a course of ten injections, the abscess was found to contain particles resembling mastic.

Acetylarsan, Specific Remedy for Lichen Planus. C. Audry, Bull. Soc. franç. de dermat. et syph. **34**:30, 1927.

Twelve cases were treated with intramuscular injections of this arsenical drug; an injection was given every five or six days, and twelve usually sufficed to complete the cure. A supplementary course of seven or eight injections is advised.

Eruptions Due to Pyrethane. Chatellier and Meriel, Bull. Soc. franç. de dermat. et syph. **34**:30, 1927.

This drug, resembling amidopyrine and antipyrine, was given by mouth, and in two cases pruritic erythematous plaques appeared.

Retarded Syphilitic Chancre: Incubation of Sixty-Three Days. J. Montpellier, Bull. Soc. franç. de dermat. et syph. **34**:31, 1927.

The patient had applied mild mercurous chloride ointment after exposure. The appearance of the chancre was followed by signs of severe spirochetemia.

Parkhurst, Toledo, Ohio.

Proceedings of the Twenty-Third Meeting of the Italian Society of Dermatology and Syphilology. Riforma med. **43**:85 and 110 (Jan. 24 and 31) 1927.

The 1926 meeting of the Italian Society of Dermatology and Syphilology was held on December 16, 17 and 18 in Rome, Prof. P. L. Bosellini presiding.

Thyroid Disfunction and Dermatosis.—Professors Artom, Bertaccini and Sparacio discussed the relation of endocrine thyroid dysfunction to certain dermatosis. They agree that except in the case of myxedema, there is no cutaneous disease that can be proved to be due directly to thyroid insufficiency.

Syphilis of the Llama.—Professors Bosellini of Rome, Lombardo of Pisa and Pasini of Milan report the results of their investigations on the Jauregui and Lancelotti theory that the South American llama was highly receptive to the syphilitic infection and that a serum could be obtained from the infected and immunized animals which had curative properties in cases of human syphilis.

Not in any case could a llama be inoculated with syphilis in Italy. Inoculations in the scrotum, the prepuce, the testicles, the eye and the vulva in the female animals were always negative.

Vaccine Therapy of Chancroid.—Maccari and Devoto report favorably on the intravenous injections of Nicolle's vaccine in the treatment of chancroid and its complications. The reactions are sometimes severe, the temperature reaching as high as 41 C. The genital lesions and buboes clear up and heal in a short time under this treatment.

Tantarelli considers this form of treatment rather dangerous in view of certain severe reactions. He believes that Nicolle's vaccine acts, not specifically, but as a foreign protein.

Malariotherapy of Early Syphilis.—Petranich of Fiume reports on the treatment of forty-seven patients with secondary syphilis with nervous manifestations and abnormal spinal fluids. He treated these patients with arsphenamine and inoculations of tertian malaria. The results were encouraging even in cases that had been resistant to treatment, especially in relapsing cases.

The Vernes Reaction.—Peli of Rome reports the result of 2,056 cases of syphilis in which he has compared the Vernes reaction with the Wassermann test. He concludes that the Vernes reaction is more sensitive than the Wassermann.

Treatment of Cutaneous Tuberculosis.—A. Radaeli has used roentgen rays, radium, the Kromayer lamp, carbonic snow and general ultraviolet light baths in ninety-four cases of tuberculosis of the skin. The roentgen rays in small doses are particularly useful in cases of lupus tumidus, vegetating and ulcerated, finishing the small resisting foci with local applications of radium. The Kromayer lamp light has little if any effect in lupus vulgaris. Carbonic snow has given good results in the treatment of lupus of the mucous membrane of the nose. The general light baths are useful as a general adjutant to the other forms of treatment.

Treatment of Lupus Erythematosus with Gold Salts.—E. Freund of Trieste has treated twenty-six patients who had lupus erythematosus with intravenous injections of different gold compounds. Fifty-two per cent of the patients were entirely cured, 22 per cent were greatly improved, 13 per cent were slightly improved and 13 per cent were unchanged. Few and unimportant reactions were observed. The author considers this the method of choice in treating this condition, but advises beginning with small doses, increasing the amount of salt slowly.

Achorion Schönleinii in Blood of Favus Patient.—Ambrosoli of Milan has consistently searched for fungi in the blood in 1,269 cases of tinea of the scalp, favus, tinea barba, etc., but recently he found and recovered in pure culture *Achorion schönleinii* from the blood of a 6 year old patient suffering from favus of the scalp. There were no allergic skin reactions in this case.

Other subjects treated at this meeting were: Syphilitic Superinfection and Immunity in Syphilis by Pasini, Sarcoid of Boeck by F. Radeli, Report of a Case of Acnitis by G. Rossi, Clinical Study of Tuberculids by Massia, Cryotherapy of Lupus Erythematosus by De Favent, Generalized Scleroderma by Tommasi, Parathyroids and the Skin by Mariani, Glycemia and Cholesterinemia in Psoriasis by Blasi, Asthma and Urticaria following Injections of Arsphenamine by Mibelli, etc.

PARDO-CASTELLO, Havana.

Society Transactions

DETROIT DERMATOLOGICAL SOCIETY

Regular Meeting, Nov. 16, 1926

ROLLIN H. STEVENS, M.D., *Presiding*

PEMPHIGUS(?). Presented by DR. BEHN.

J. H., a boy, aged 3 years and 6 months, had a vesicular and bullous eruption, especially on the trunk, which had first appeared ten months before presentation. New lesions had appeared from time to time. There had been no visible lesions of the mucosa, nor was there any pruritus. There was little pigmentation.

DISCUSSION

DR. BIDDLE: This appears to be a case of pemphigus.

DR. WIEDER: Might this not be in a group between erythema multiforme bullosum and pemphigus? A focus of infection may be found in this case.

DR. SHAFFER: This case seems to shade into the erythema multiforme group.

DR. BEHN: There is a nasal focus of infection.

DR. JAMIESON: This is not dermatitis herpetiformis. Pruritus is not present. The patient acts like a sick child. It is apparently not a case of erythema multiforme, but appears to be pemphigus.

LINGUA NIGRA. Presented by DR. WOLLENBERG.

A man, aged 50, had first noticed a "black coating" on his tongue three weeks before presentation; it had remained unchanged. The affected area was lozenge-shaped, occupying the posterior two thirds of the dorsum of the tongue; it was jet-black, and the papillae were uniformly elongated. The patient had not taken iron or any other medication.

DISCUSSION

DR. BIDDLE: The onset was too sudden for lingua nigra, and the surface is too moist.

DR. BREITENBACH: The patient has been using a mouth-wash. Might this not be causative?

DR. SHAFFER: Cultures should be made. The length of the papillae favors a diagnosis of lingua nigra.

LICHEN PLANUS HYPERTROPHICUS. Presented by DR. SCHILLER.

S. K., a man, aged 33, born in Europe, had had severe pruritus of the genito-crural region for ten months. The skin of the entire area was violaceous, uniformly thickened, and excoriated and crusted in places. The blood picture and urinalysis presented a normal condition, and vegetable parasites were not found in scrapings.

DISCUSSION

DR. PARKHURST: I could not find any lichen planus papules in this case, and would therefore suggest a diagnosis of neurodermatitis.

A Case for Diagnosis. Presented by Dr. Troxell.

P. M., a negro, aged 47, born in Mississippi, presented a large pea-sized, flat, indurated nodule on the left side of the tongue. It had been present for two years, but had gradually increased in size, and was said to be more noticeable when the patient smoked heavily.

DISCUSSION

Dr. Parkhurst: The nodule is firm, and gives the impression of a cyst undergoing calcareous change.

Dr. Shaffer: I agree with Dr. Parkhurst, and would recommend excision.

A Case for Diagnosis: Rhinoscleroma (?). Presented by Dr. Jamieson.

L. L., a Russian, aged 50, a butcher, was in good general health and had six healthy children. About two years before presentation, he had had erysipelas and a carbuncle on the neck, followed by a small suppurating lesion on the tip of the nose, which never entirely disappeared. The lesion slowly enlarged, became hard and painless, and reached a diameter of 1 cm. Following a diagnosis of epithelioma, radium needles were applied twice, and following this, ulceration occurred and persisted, but was superficial. Wassermann reactions had been negative repeatedly. Neither biopsy nor smears had been made.

DISCUSSION

Dr. Shaffer: Was there any infiltration of the mucosa?

Dr. Jamieson: None has been found.

Dr. Parkhurst: I recall a case seen several years ago, apparently almost identical with this one, in which the possibility of syphilis, tuberculosis and rhinoscleroma was considered; biopsy examination showed it to be an endothelioma.

A Case for Diagnosis. Presented by Dr. Perkins.

J. F. M., a man, aged 50, a laborer, born in America, had first noticed lesions on the forehead about a year before presentation. The eruption had involved the entire forehead, the left cheek and the left side of the neck, with more or less infiltrated erythematous papules varying in size from that of a large coin to small palm-sized circinate and gyrate arrangements. There was some central scaling and pigmentation. Microscopic examination was said to have shown "a fungus growth"; the Wassermann reaction was negative.

DISCUSSION

Dr. Wollenberg: There is a marked resemblance to syphilis, but the eruption first appeared quickly as an erythema, with necrotic papules. It may be lupus erythematosus.

Dr. Shaffer: There are follicular plugs, and I would favor a diagnosis of lupus erythematosus, or possibly sarcoid. I would suggest biopsy.

Dr. Parkhurst: The infiltration of the papules would suggest a diagnosis of syphilis or sarcoid rather than lupus erythematosus.

Dr. Bartholomew: I favor a diagnosis of syphilis.

A Case for Diagnosis. Presented by Dr. Stevens.

L. H., a man, aged 30, had first noticed an eruption on the flexure of the forearm nineteen days before presentation. It gradually became generalized, the elementary lesion being a small erythematous papule. The fauces were erythematous, and there was a grayish membrane on the gums which could be detached without bleeding. The axillary lymph nodes were palpable. There was some malaise, but a normal temperature. Gradually the eruption became macular and exfoliative, resembling seborrheic dermatitis, and this was the appearance at the time of presentation. The patient had been delivering fuel oil for two months prior to the onset of the eruption. He had used ethyl gas in the motor of his truck, and had constantly inhaled the fumes from a leaking exhaust pipe. It was thought that either the oil or the exhaust gas might have been the etiologic factor.

DISCUSSION

Dr. Bartholomew: Within the past month I have seen three oil station employes with a similar dermatitis.

Gumma of the Chest. Presented by Dr. Van Rhee.

J. U., a millwright, aged 40, presented a discharging sinus at the left side of the upper sternum, and numerous scars over the sternum and right side of the chest. The lesions had appeared four years previously, following an injury by a piece of heavy iron bar. The Wassermann reaction was positive. There was also laryngitis.

Verrucae Planae Juveniles. Presented by Dr. Troxell.

J. H., a schoolgirl, aged 8 years, presented a large number of flat warts, many with linear arrangement, on the hands, wrists and face, of five years' duration.

DISCUSSION

Dr. Biddle: I would suggest that sulpharsphenamine be given intramuscularly, as advised by Dr. Sutton of Kansas City.

Dr. Van Rhee: We have failed to obtain satisfactory results with sulpharsphenamine in five cases.

Dr. Perkins: Sulpharsphenamine is apparently more effective against warts in adults than in children.

Dermatophytosis of the Breast. Presented by Dr. Troxell.

Mrs. B. C., a negress, aged 22, had had a moist erythematous patch involving the areola for three months. There was a similar patch on one leg. An organism had not been found.

Flat Condylomas. Presented by Dr. Van Rhee and Dr. Behn.

Mrs. M. C., aged 46, presented a generalized maculopapular eruption, with mucous patches on the anterior faucial pillars and many flat copper-colored papules on the inner surfaces of the thighs and the perineum. The eruption was of two weeks' duration, and the Wassermann reaction was strongly positive.

Annular Syphilid. Presented by Dr. Schlegelmilch.

Mrs. R. McF., a white woman, aged 22, presented a generalized annular papular eruption, the rings being medium coin-sized, with infiltrated borders.

The tonsils were inflamed, and vaginal examination showed a cervical erosion. The Wassermann and Kahn reactions were strongly positive.

MORPHEA IN SISTERS. Presented by DR. VAN RHEE.

One young girl presented a large coin-sized, pale, thickened patch, with violaceous border, on the abdomen, and the other girl had several pale, slightly atrophic, large coin-sized patches on the knees and legs.

DISCUSSION

DR. WIEDER: We saw these cases at Ann Arbor four months ago, and diagnosed the abdominal lesion as early morphea, and the leg lesions as more advanced morphea.

A CASE FOR DIAGNOSIS. Presented by DR. JAMIESON.

Mrs. C., aged 52, a widow, had had an intensely pruritic eruption for fourteen months, consisting of dark erythematous plaques, with a thin scale, on the palms, elbows, extensor surfaces of the forearms and dorsa of the hands and first phalanges. The finger-tips were sensitive. The patient was excitable and easily fatigued.

DISCUSSION

DR. PARKHURST: The appearance is not that of an occupational eruption, of dermatophytosis or of psoriasis. There are a few small polygonal papules, which, with the pruritus, suggest a diagnosis of lichen planus.

DERMATOPHYTOSIS OF THE NAILS. Presented by DR. SCHILLER.

Mrs. S. B., a Jewess, aged 28, had had the condition for one year. There was a patch of small vesicles on the right palm, and the nails of both hands were rough and pitted. Scrapings were examined with negative results.

A CASE FOR DIAGNOSIS. Presented by DR. VAN RHEE and DR. BEHN.

Mrs. M. W., aged 30, presented a purplish, olive-sized tumor on the dorsum of the tongue. It was lobulated, the anterior part being indurated and the posterior portion being pedunculated, freely movable and apparently hemangiomatous. The tumor had first appeared twenty-one years previously, after the patient had bitten and lacerated her tongue.

DISCUSSION

DR. SHAFFER: This tumor appears to be a fibro-angioma.

URTICARIA PIGMENTOSA. Presented by DR. VAN RHEE and DR. BEHN.

A. S., a Jewess, aged 16, presented reddish brown macules, of general distribution. When the lesions were irritated, wheals appeared, with pruritus. The eruption was of one year's duration.

DISCUSSION

DR. WOLLENBERG: It is unusual for urticaria pigmentosa to develop at this patient's age.

DR. JAMIESON: This is apparently a case of chronic urticaria with pigmentation.

DR. SHAFFER: I have seen a similar case, in which the eruption was found to be caused by phenolphthalein.

DR. PARKHURST: The patches of phenolphthalein eruptions which I have seen have all been much larger than these. In this case the macules give rise to wheals when stroked, and I would accept the diagnosis of urticaria pigmentosa of the adult type.

DR. BIDDLE: The distribution of the lesions is remarkably sparse.

DR. VAN RHEE: A biopsy examination will be made and the results reported later.

ANNULAR SYPHILID. Presented by DR. VAN RHEE and DR. BEHN.

Mrs. A. W., a negress, aged 20, presented annular papular lesions at the angles of the mouth, externally and internally, and on the tongue. The lesions were of seven months' duration. The Wassermann reaction was strongly postive.

H. J. PARKHURST, M.D., Reporter.

CHICAGO DERMATOLOGICAL SOCIETY

Regular Meeting, Nov. 17, 1926

DR. PAUL A. O'LEARY, *Presiding*

LUPUS MILIARIS FACEI. Presented by DR. OLIVER and DR. FINNERUD.

A negress, aged 24, had an eruption of the skin of the eyelids in the vicinity of the inner canthi, on the center of the chin and angles of the mouth, of one year's duration. There were no subjective symptoms. She believed that the lesions of the eyelid appeared before those in the other areas. There had been no previous disorder of the skin. So far as she could tell, the lesions were at a standstill, and none had disappeared. She had received no treatment other than a salve suggested by her druggist. She had always been in good health, and there was no family history of tuberculosis or other disorders of special interest. She had been married seven years and had had one pregnancy, six years ago, which terminated in an abortion at seven months following severe exertion. The child was born alive, but died a few minutes after birth.

Examination showed from six to a dozen or more pinhead-sized follicular nodules in each of the areas mentioned. Some of the lesions contained a central horny plug. The mucous membranes of the mouth were normal. A biopsy was unobtainable.

DISCUSSION

DR. OLIVER: I think this case belongs to the group described by Wise and Eller as lupus miliaris disseminatus facei.

DR. ZWICK: A Moro test is at times a useful diagnostic aid in dubious cases. Because the condition occurs so generally subsequently to or in connection with the acute exanthemas, especially measles, this form of lupus vulgaris is frequently called lupus postexanthematicus in Europe. It is interesting that, concurrent with the hematogeneous dissemination to the face, multiple miliary foci may develop in the lungs and are revealed by roentgen-ray examination.

TUBERCULOSIS OF THE TONGUE. Presented by DR. OLIVER and DR. FINNERUD.

A man, aged 42, complained of two sores on the tongue of eight months' duration. The lesions began as cracks at the margin of the tongue and slowly increased in size. He gave a history of having received treatment for the past year for pulmonary tuberculosis.

Examination showed two finger-nail-sized ulcers of the margin of the tongue, one near the tip and another well back on the left side. The lesions had a slightly papillomatous base, and the margin was somewhat undermined. They were rather soft, but firmer than the surrounding normal tissue of the tongue. Smears of the sputum, prepared by Dr. J. T. Belting of the Cook County Hospital, showed acid-fast bacilli of the structure of tubercle bacilli.

DISCUSSION

DR. MICHELSON: It is important in these cases to point out that the prognosis as to life is unfavorable, because the condition usually occurs in patients with advanced tuberculosis. Frequently the pain associated with these ulcers can be relieved by means of acid mercuric nitrate.

DR. FOERSTER: In order to make the diagnosis positive it is important to get the bacteria in the scrapings of the lesions.

DR. FINNERUD: *Bacillus tuberculosis* was recovered from the surface of the ulcer in this case, but it was thought that the organisms demonstrated were really from the sputum. The patient had an active infection, and all specimens of sputum were positive. From the clinical standpoint, the wedge-shaped ulcers and their papillomatous surface were among the characteristics of tuberculosis of the tongue.

DR. FOERSTER: Another characteristic point in this case is the scalloped margin, which is produced by broken-down miliary tubercles.

DR. ZWICK: One characteristic is the festooned outline of the tissues forming the eroded, overhanging or undermined borders of the ulcer, beneath which the bacillus of Koch may usually be demonstrated. Another characteristic feature is the so-called "yellow grains" of Trélat, which is absent in this case just now.

CHLOASMA IN A MAN. Presented by DR. OLIVER and DR. FINNERUD.

A man, aged 30, a mechanic for the past seven years, complained of brown spots on the sides of the cheeks and on the bridge of the nose of one year's duration. He said that the lesions had never been reddish or any other color, and his impression was that the patches on the cheek were increasing in size. He had noticed that the patches were a darker brown during the last summer than at any other time, and thought they were now becoming paler. He had always been troubled with chronic constipation, but otherwise his general health was good. He had not received treatment.

Examination showed almost identically outlined patches of light brown pigmentation of the sides of the cheeks and bridge of the nose. The areas on the cheek were 2 or 3 inches (5 by 7.6 cm.) in diameter. Although the patient's complexion was rather ruddy, telangiectases were more numerous and more distinct in these patches than elsewhere.

DISCUSSION

DR. PUSEY: I think that chloasma is the proper diagnosis in this case, and yet it is not a typical picture. I would not have given it that name, yet would have

had no other to suggest. I think the coffee-colored spots are not uncommon in men with telangiectatic skin.

DR. MITCHELL: The telangiectasis was more pronounced in the lesions than in other parts of the face.

DR. FOERSTER: I agree with the diagnosis of chloasma.

DR. FINNERUD: As was noted in the history, this man has always had a ruddy complexion. The telangiectases were more marked on the nose and in the pigmented lesions on the cheeks than elsewhere. For that reason an attempt was made to get a history of erythema, with the thought of superficial lupus erythematosus as a possibility. The absolute symmetry of the lesions is remarkable.

A CASE FOR DIAGNOSIS. Presented by DR. ZEISLER.

A physician, aged 28, complained of a lesion on his nose which had been present for three weeks. It began as a small papule, but had gradually enlarged to 1 cm. in diameter, with a well marked inflammatory border and depressed center. He had been in good health and had not taken any medicine.

DISCUSSION

DR. FOERSTER: I think that this condition is lupus erythematosus of the early discoid type, showing the usual characteristics. I believe further that in isolated lesions of this type we should rule out the possibility of their being due to the ingestion of coal tar products. The lesions caused by these drugs may closely simulate lupus erythematosus.

DR. ZWICK: I hope that Dr. Zeisler will report to us later his conclusions about the two small lesions on the right cheek. They impress me as being possibly the beginning of a lupus erythematodes.

DR. PUSEY: I agree with the diagnosis, but I think that it must be made by exclusion at the present time. The lesion is edematous, and its absolute isolation is peculiar.

MULTIPLE EPITHELIOMAS. Presented by DR. STILLIANS.

A widow, aged 35, first noticed a growth on the left ala nasi at the age of 26. Three years later this was excised, leaving a large defect. She then consulted the late Dr. F. G. Harris, who treated the borders of the opening with the roentgen ray, and Dr. William R. Cubbins performed a plastic operation. At that time she had a papule on the bridge of the nose. Two months before presentation two small ulcers appeared on the right ala. The smaller of these, about 0.3 by 0.5 cm., was shallow and had no perceptible nodules on its border. The larger ulcer was also shallow, about 0.7 by 1 cm., and on its lower border were several papules about 0.2 cm. in diameter. These lesions and the papule on the nasal bridge had received nine units of the roentgen ray each, and consisted of erosions surrounded by a sharply defined erythematous halo. On the right cheek near the nose was an untreated papule, 0.5 cm. in diameter and about 0.3 cm. high, translucent pink, with dilated arterioles over its top. The large plastic area, filling the former defect in the left ala, was bright yellow, in sharp contrast to the color of the rest of the face.

A CASE FOR DIAGNOSIS. Presented by DR. SENEAR and DR. WIEN.

This patient was presented at the October, 1926, meeting of the Society and was shown again at the request of some of the members who thought last

month that the lesions about the eyes were due to the application of a caustic. No treatment had been used during the interim, and the picture remained unchanged.

DISCUSSION

DR. FINNERUD: I think, as I did last month, that the condition about the eyes is lupus erythematosus, precipitated by the use of the irritant applied to the patches of xanthelasma. I think that the lesions of the buccal mucous membrane are more typical of lupus erythematosus than they were last month, because of the increased erosion of their centers. The lesions on the wrists and back of the hands are hard to account for and, taken alone, would be diagnosed lichen planus, but the man has some senile warts on the hands, and I believe that these sometimes take on the appearance of lichen planus.

DR. ZEISLER: This case is unique and should be reported in full. I feel that the lesions on the hands are typical of lichen planus and that those of the mucous membranes and eyelids belong to the same disease. I see no reason for looking for two different conditions to explain the clinical picture.

DR. DRIVER: I thought that the lesions on the mucous membrane were those of lupus erythematosus and that those about the eyes were lichen planus atrophicans.

DR. ZWICK: One group of lesions consists of typical xanthelasma palpebrarum. But the interpretation of the rough, grayish-white cretaceous incrustations present some difficulty, because the original appearance seems to have been modified by treatment, although the therapeutic measures apparently have been nothing more than applications of hot chamomile infusion. I am inclined to consider the diagnosis of lupus erythematosus. The simultaneous presence of the two diseases of the skin may be a coincidence.

DR. FOERSTER: I agree with Dr. Finnerud that the lesions of the mucous membranes are clinically those of lupus erythematosus. It is true that a network-like arrangement is present, but there are no nodal swellings at the points of intersection, and in some places there are the peculiar fanlike striations of lupus erythematosus. The lesions on the lips also resemble those of lupus erythematosus. If these extensive lesions of the buccal mucosa and lips were those of lichen planus, definite changes in the tongue could be expected also. In lupus erythematosus the absence of lesions on the tongue would not be uncommon. The papules on the hands show milky striae and it may be that two conditions are present in this case.

DR. STILLIANS: I think that the peculiar combination of symptoms in this case is more easily explained as lichen planus than as lupus erythematosus. I know of a case of lichen planus that was seen by the late Dr. Hyde, which has lasted for twenty years.

DR. PUSEY: The last time this patient was presented I agreed with the diagnosis of lupus erythematosus, but the lesions on the flexor surfaces of the wrists now are characteristic of lichen planus. I have never seen anything like the lesions about the eyes, but I accept a diagnosis of lichen planus, although a ring of lichen planus about the eyelids is peculiar, replacing as it does the xanthelasma in this location.

DR. SENEAR: I have under observation at present a patient who has had lichen planus limited to the mucous membranes of the mouth and to the glans penis for at least twelve years. I have seen him from time to time during the past ten years, and before that time he was under the care of Dr. Fred Harris

for several years. I have been unable to reach a definite decision in regard to the present case as to which of the two conditions discussed is represented. I hope to admit the man to the hospital and to secure material for microscopic study.

A Case for Diagnosis. Presented by Dr. Ebert.

A man, aged 31, nine weeks previously had developed a painless swelling of the left side of the neck anterior to the digastric muscle. Two weeks later his tongue became somewhat swollen and the tip of the tongue raw, but the condition caused him no discomfort at first. Hot dressings were applied to the neck, and an abscess pointed, which was incised by his physician. Considerable greenish pus was discharged. The swelling of the neck gradually diminished in size, and two weeks later ceased draining. Three weeks ago the patient was admitted to the Cook County Hospital, where his Wassermann reaction was found to be two plus. He was given five injections of neoarsphenamine and four mercurial inunctions. This helped the tongue very little, and considerable gingivitis developed following use of the mercury. At the time of presentation he could take only liquid nourishment and had lost 50 pounds (33.7 Kg.) or more. He gave a history of having had gonorrhea seven years ago, but said that he had not had a chancre.

The tongue was swollen to three times its normal size. There was considerable salivation and some gingivitis. Erosions and shallow ulcerations were present on the anterior half of the tongue, two or three of which were covered by an adherent yellowish-white membrane. The tonsils were infected. In the anterior triangle of the neck there was a firm gland the size of a walnut, which was attached to the skin by scar tissue. The Wassermann reaction was negative. Dark-field examination of the preparations from the tongue and from a puncture of the gland were also negative. Vincent's organisms were not demonstrated in any of the smears from the tongue, nor were fungi. The patient had been given daily injections of sodium hyposulphite and a mouth wash since his admission to the dispensary. The differential blood count was practically normal.

DISCUSSION

Dr. Michelson: Carcinoma, syphilis and tuberculosis may be excluded because of the acuity of the process, and I think thrush should be sought. With a tongue like this associated with enlarged glands I think that operation should not be delayed. A patient of mine with a similar condition developed a postpharyngeal phlegmon and died before I was able to make up my mind as to the proper procedure. It is important not to delay drainage of the glands in these cases.

Dr. Mitchell: I have seen two cases of disease of the tongue with a somewhat similar appearance in which no adenopathy was present. The cases were investigated thoroughly from the bacteriologic standpoint, but the results were negative.

Dr. O'Leary: The possibility of lymphosarcoma should not be forgotten in this case. It has been impressed on me several times that lymphosarcoma may manifest itself in this location. A biopsy of a gland would be of value, particularly if the adenopathy persists.

Dr. Senear: I have under observation at the hospital at present a patient with a small ulcer on the frenulum of the tongue. Shortly after this appeared he developed a submaxillary adenopathy, and later the posterior cervical and

mediastinal glands were involved. As he has a positive Wassermann reaction, antisyphilitic therapy had been employed before I saw him, without any effect. One of the glands in the neck became softened, and a pure culture of *streptococcus viridans* was obtained by aspiration. The ulcer in the mouth likewise yielded the *streptococcus viridans*. The picture originally suggested a possible Hodgkin's disease, the softening of the gland possibly being due to secondary infection. The patient is improving rapidly, however, and the entire condition is apparently due to the streptococcic infection.

DR. FOERSTER: With the history of a thick, adherent membrane and the presence of enlarged glands, it is advisable to consider the possibility of diphtheria in the differential diagnosis of this case. Diphtheria of the skin is a familiar condition and it might easily occur in the locations involved here.

PIGMENTATION OF THE FOOT. Presented by DR. H. M. HEDGE.

A white youth of American birth, aged 19, employed in an ice cream factory, said that for the past five years he had had pigmented spots on the lateral aspect of the right foot, beginning about 10 cm. above the right malleolus and extending distally to the toes and somewhat in between them. The lesions followed in a general way the course of the small saphenous vein and along the venous arch of the dorsum of the foot. Above the malleolus was a deeply indurated area which seemed more or less adherent to the deeper structures. The patch below the malleolus contained deep-seated varices, with some nodules. Further down toward the toes and on the dorsum of the foot the veins could be palpated; the pigmented areas were much more superficial and surrounded by small discrete spots from 1 to 3 mm. in diameter. There was some scaling over all the areas and considerable swelling of the foot and lower part of the leg. There also was some elevation of temperature in the right leg.

The patient gave a history of a minor trauma nine years before, when he ran a nail into the bottom of the foot. It had pierced the metacarpal region and emerged from the dorsum. The wound healed after two or three months, following considerable discharge of pus, but no fragments of bone. There was also a ringworm infection of the toes. The Wassermann reaction was negative. Photographs and a biopsy were presented.

DISCUSSION

DR. ZEISLER: I wish to offer the diagnosis of multiple idiopathic hemorrhagic sarcoma, Kaposi.

DR. FINNERUD: From the microscopic picture, I think that Kaposi's sarcoma is probable. On the dorsum of the toes at their sides there is a verrucous element, which might possibly be related to intertriginous ringworm infection, but which is also characteristic of Kaposi's sarcoma when the lower half of the leg is involved to a considerable extent.

DR. PUSEY: It is my impression that the condition is a beginning of Kaposi's sarcoma, with characteristic infiltration, warty change and pigmentation.

LUPUS ERYTHEMATOSUS IN A NEGRESS. Presented by DR. OLIVER and DR. FINNERUD.

A colored girl, aged 19, had an eruption of the face and scalp of ten years' duration, which was practically devoid of subjective symptoms.

Examination showed a typical eruption of lupus erythematosus of the discoid type on the face and in the scalp in the region of the vertex. There were no lesions in the mouth and none on the body.

SARCOMATOSIS CUTIS (MYCOSIS FUNGOIDES D'EMBLÉE). Presented by DR. FREDERICK SCHMIDT.

A white man, aged 60, had not suffered from any skin trouble except itching on the back of the hands after touching gasoline. One year previous to presentation some red lumps appeared on the right shoulder, without itching or pain. A few months later more lesions appeared, and by June a large ulcer had formed in this locality. He entered the hospital in August, with tumors scattered over the body. Itching had been absent. The urine and blood were normal, and the Wassermann reaction was negative. There were numerous sharply demarcated tumor-like growths varying in size from that of a pea to that of a thimble, scattered over the body, solitary and in groups. The majority of these lesions were elevated, rose-violet, and covered with a smooth epidermis, but some had undergone central eczematization. Red-brown areas marked the site of lesions which had disappeared. There was an area of new, red skin, 9 by 6 cm. on the right shoulder, containing two dime-sized ulcers. In a section of a node removed from the left forearm there was a dense infiltration of large, irregularly rounded cells, arranged in packets separated from one another by connective tissue, filling the entire corium and upper portion of the subcutis. The nuclei showed frequent mitoses and a high chromatin content, and only in the subcutis did the cells resemble normal lymphocytes. There was marked swelling of the collagen, and a section stained with resorcin fuchsin, after Pronter, showed clumping of the elastic fibers in the papillary body.

DISCUSSION

DR. MICHELSON: I think the cases in the group of sarcomatosis cutis should be followed to the end and reported. I have a patient in Minneapolis at present with a similar picture, and Professor Gans said that from the microscopic standpoint the condition was sarcoma, but with regard to prognosis he had nothing to say, for that could not be decided from the microscopic picture alone.

DR. ZWICK: Having observed severe toxic symptoms after heavy roentgen-ray treatment in cases of this type, I have become rather cautious. I would suggest in the present case the avoidance of massive doses. The absorption of the protein of the tissues, rapidly destroyed by the roentgen ray, was followed by the death of the patient in a case which I saw recently.

DR. PUSEY: I think I have spoken here before of the case of carcinoma en cuirasse of the breast which I saw and in which the condition looked as though the patient might be expected to die within three months. The condition cleared up under roentgenotherapy, but the patient returned in about eight months with a shower of carcinomas all over the skin, in the mediastinal glands and elsewhere. She was given more roentgenotherapy as a placebo. Much to my surprise, she returned in six months and most of the lesions had disappeared. Although some lesions are still present, there has been a spontaneous remission of her generalized carcinomatosis.

DR. O'LEARY: I have had under observation a patient who first presented a carcinoma en cuirasse. The left side of the anterior chest was definitely infiltrated. She received intensive roentgenotherapy, and the pigmentation following application of the roentgen ray extended down to the umbilicus.

When seen several months later, she presented an extensive carcinomatosis cutis confined, however, only to the areas of pigmentation which the roentgen-ray therapy had produced. The demarcation at the borders of the pigmentation was distinct and, I thought, rather unusual. At the time of the second visit a roentgenogram of the chest showed a fibrosis of the lungs.

DR. FREDERICK SCHMIDT: The genetic relationship between lymphosarcoma, mycosis fungoides and leukemia is such that they might be grouped together, but lymphogranulomatosis should be kept in a category by itself.

DR. FINNERUD: A patient with mycosis fungoides who died recently at the Cook County Hospital presented lesions of sarcoma type in the spleen and liver at necropsy, while the general cutaneous picture was similar to that presented by this patient. In the present case the microscopic picture is that of mycosis fungoides in the epidermis and upper corium, while that in the deeper part of the corium and the hypoderm is identical with the picture described by Fraser. Here there are numerous large cells with mitoses.

DR. O'LEARY: Has anyone had any experience with the use of Coley's serum in the treatment of sarcomatosis cutis?

DR. PUSEY: I had years ago some experience with this treatment and found that if one uses doses of Coley's serum sufficient to get a reaction retrogression of the tumors takes place, but I have never seen any permanent improvement result.

ERYTHEMA INDURATUM. Presented by DR. STILLIANS for DR. ROSENBERG.

A negress, aged 27, had been treated at the Health Department Clinic with mercurial inunctions until her gums became sore. She was then admitted to the Cook County Hospital, where she received ten intravenous injections of neoarsphenamine. She was then discharged and referred to the Northwestern University Clinic for further treatments. On admission she gave a negative Wassermann reaction and was given injections of potassium bismuth tartrate, 0.1 grain (0.006 Gm.) once a week for ten weeks. This therapy had little influence on the lesions.

Roentgenographic examination showed no osteomyelitis in the involved area and no evidence of disease of the chest.

The lesions practically encircled the lower third of both legs and consisted of infiltrated patches, with scattered nodules, some of which had undergone ulceration. Some of the ulcers had healed, leaving hard, adherent scars.

Biopsy revealed marked infiltration in the corium of round cells with proliferation of fibroblasts and numerous giant cells of the Langhans type.

PITTSBURGH DERMATOLOGICAL SOCIETY

Regular Meeting, Nov. 18, 1926

F. M. JACOB, M.D., *Presiding*

EPULIS. Presented by DR. BEINHAUER.

Mrs. M., aged 45, presented a growth involving the upper left anterior margin of the hard palate. The patient said that the lesion had been present for four months and closely followed a series of ulcers caused by an ill fitting

plate. To date, subjective symptoms had been lacking entirely. An oval shaped, dusky-red, almond sized lesion which caused a protrusion of the upper lip was found beneath the upper lip, extending from the midline toward the left side. The lesion was hard, painless and attached over the area of the left incisor fossa by a small pedicle allowing rather free motion. The lesion was single and lobulated and presented a studded nodular surface covered by a smooth shiny epithelium. To the right of the midline along the anterior ridge of the palate were a series of shiny pea-sized nodular lesions not unlike the larger one. No apparent glandular enlargement was present. The blood Wassermann reaction was negative.

DISCUSSION

DR. GUY: I wish to offer a diagnosis of epulis, but I do not wish to commit myself as to its relative malignancy. Dr. Jacob and I have removed three of these growths during the past year, and in two instances the general pathologist was unwilling to admit any malignancy, and the other one showed a slow growing giant cell sarcoma. Removal, with the electric knife and radium has been successful in all three cases, to date.

DR. WERTHEIMER: I believe that the growth is malignant.

DR. HOLLANDER: I believe the growth is a malignant epulis because of its firmness, vascularity and color. These lesions usually follow trauma and should be removed by electrocoagulation followed by radium implants.

DR. BEINHAUER: I believe that the lesion is an epulis, but I cannot dismiss the question of malignancy. I expect to remove the mass with the cautery knife and follow up with radium treatment. I shall present a microscopic report at the next meeting. (The biopsy showed an epulis.)

A CASE FOR DIAGNOSIS. Presented by DR. SCHWARTZ and DR. BUSMAN.

S. Z., a school girl, aged 17, presented an eczematous dermatitis of the neck and shoulders. The condition began four years before presentation and had never been entirely well. Her general health was normal. Areas of lichenification, erythema, pigmentation, scaling and some oozing, were scattered diffusely over the neck and shoulders. The individual lesions were flat, shiny papules which were grouped in patches representing the oldest lesion present. The early lesions were erythematous, then papulovesicular.

DISCUSSION

DR. HOLLANDER: I consider this a case of lichen simplex chronicus because the type of the lesion, the distribution, the peculiar shiny appearance and pigmentation more closely simulate the latter condition.

DR. BUSMAN: I favor a diagnosis of metabolic eczema resulting from an endocrine disturbance, and I would treat the patient accordingly. Although the character of the lesions favors the diagnosis of lichen simplex chronicus, I believe the distribution is against it.

PELLAGRA. Presented by DR. HOLLANDER.

A man, aged 38, unmarried, presented a fading eruption of a dry dermatitis resembling sunburn which was symmetrical, glove-like and involved the extremities. The patient had marked gastro-intestinal disturbance and symptoms of cerebrospinal disturbance.

DISCUSSION

DR. GUY: I have seen this patient during two attacks and he had dementia, dermatitis and diarrhea. The mental condition is now materially worse, and the prognosis is bad.

DR. HOLLANDER: I have attended the patient for only a few days and cannot note any improvement in his condition.

PEMPHIGUS FOLIACEUS. Presented by DR. HOLLANDER and DR. FISHER.

S. L., aged 27, colored, unmarried, presented on the trunk, both anteriorly and posteriorly, an encrusted discrete and confluent, foul-smelling eruption. The lesions were crusted and represented dried bullae. A few flaccid pus-containing lesions with ulcerative tendencies were scattered over the extremities. The mucous membranes were normal. The blood Wassermann reaction was negative.

DISCUSSION

DR. HOLLANDER: This patient has been treated at a urologic dispensary during the past nine months for syphilis. I am going to try blood transfusions and will report their effect at a later meeting.

LUPUS VULGARIS. Presented by DR. PHILLIPS.

A. M., a housewife, aged 26, presented a lesion involving the entire right cheek. The lesion was circular, with a healed scar in the center and an active periphery which was studded with numerous apple jelly nodules. The lesion had been present for nineteen years and began as a single pea-sized nodule. To date, thirty exposures to the roentgen ray had been given without any appreciable therapeutic effect. The physical examination with the exception of enlarged cryptic tonsils and a few decayed teeth was negative. There was not any evidence of pulmonary tuberculosis.

DISCUSSION

DR. WERTHEIMER: I advise curettage of the individual nodules followed by the application of powdered potassium permanganate crystals.

DR. HOLLANDER: I believe that it is poor surgical practice to curet an active tuberculous process, and I advise curettage only after the tissue in question has been devitalized by electrical desiccation or cauterization.

DR. PHILLIPS: I have been using the Kromeyer lamp with pressure, and the condition is gradually improving.

A CASE FOR DIAGNOSIS. Presented by DR. GUY and DR. JACOB.

A woman, aged 49, presented an eruption of one year's duration, involving the left hand. The index finger presented an atrophic scarring, the result of healing of the process which began on the terminal phalanx. At the base of the finger on the dorsal surface of the hand was a dollar-sized scaly and crusted area with an elevated somewhat verrucous border and depressed center. A similar but smaller lesion was seen on the last phalanx of the middle finger. The Wassermann reaction was negative. Section of the tissue revealed a verrucous epidermis with a nondescript heavy infiltration in the corium. (Subsequent investigation revealed an advanced pulmonary tuberculosis, and a second biopsy agreed with the first except that there were areas suggesting beginning

malignant degeneration. The arrangement of the infiltration suggested the possibility of tuberculosis but was not definite, and tubercle bacilli could not be found).

DERMATITIS VENENATA. Presented by DR. HOLLANDER.

T. N. L., a man, aged 26, presented an acute inflammatory vesicular eruption involving the neck, shoulders, axillae, elbows and forearms. A confluent lichen-like appearance was seen on the neck, while on the shoulders, upper forearms and arms the eruption was plaquelike, bordered by fine minute vesicles following closely the lines touched by the seams of his wearing apparel. The eruption had been present two weeks; he had had a similar attack in June, 1926. There were no lesions where the body was protected by the underwear. At the time of each of these attacks the patient had worn the same sort of tan shirt.

DISCUSSION

DR. PHILLIPS: I agree with the diagnosis, and I am interested in knowing what the irritant factor is.

DR. MILLER: I wish to cite the clinical resemblance of this case to one of barberry dermatitis which was seen at the meeting of the Cleveland society.

DR. HOLLANDER: The eruption is unusual in my experience, and its distribution suggests the diagnosis. An attempt will be made to ascertain the nature of the irritant factor.

HERPES ZOSTER. Presented by DR. HOLLANDER and DR. BAER.

Mrs. H. J. C., aged 18, presented a linear eruption on the left thigh, abdomen, chest and shoulder. A cluster of lesions grouped in a fan-shaped arrangement was found on the left side of the abdomen, midway between the umbilicus and the symphysis pubis. Directly above, under the left breast, was a linear arrangement. These lesions were connected by a straight line of lesions carried down along the midline toward the left. A similar linear lesion could be seen posteriorly on the left buttock and extending downward over the posterior aspect of the knee to the foot. It was difficult to demonstrate vesicles in the lesions which were suggestive of lichen planus papules. The eruption was of one week's duration and was preceded by mild prodromal symptoms of a "head cold." An accompanying neuritis was demonstrated on deep pressure over the areas of involved skin.

DISCUSSION

DR. BUSMAN: I cannot think of any condition other than herpes zoster which could produce this picture.

DR. HOLLANDER: I have never seen a similar eruption. The tendency toward vesiculation and the associated neuritis together with the history of prodromal symptoms cause me to believe that this is a case of herpes zoster.

ADDITIONAL CASES

CORNU CUTANEUM. Presented by DR. WERTHEIMER.

MOLLUSCUM CONTAGIOSUM. Presented by DR. WERTHEIMER.

CANITIES. Presented by DR. AMSHEL.

SYPHILIS. Presented by DR. SCHWARTZ and DR. BUSMAN.

CASE FOR DIAGNOSIS. Presented by DR. SCHWARTZ and DR. BUSMAN.

DERMATITIS PAPILLARIS CAPILLITII. Presented by DR. WERTHEIMER.

LICHEN SCROFULOSORUM. Presented by DR. WERTHEIMER.

EPITHELIOMA. Presented by DR. BEINHAUER.

PAPULO-NECROTIC TUBERCULIDE. Presented by DR. SCHWARTZ and DR. BUSMAN.

SECONDARY SYPHILIS. Presented by DR. GUY and DR. JACOB.

L. G. BEINHAUER, M.D., Secretary.

NEW YORK DERMATOLOGICAL SOCIETY

Regular Meeting, Nov. 23, 1926

H. H. WHITEHOUSE, M.D., *President*

CAVERNOUS HEMANGIOMA. Presented by Dr. Fraser.

D. M., a boy, aged 14 months, presented a bluish red, elevated, oval-shaped (three and one fourth inches by one seventh inch [8 cm. by 0.3 cm.]) spongy mass on the cranial surface of the left pinna, which had been present since birth. Carbon dioxide snow had been applied three times without benefit.

An expression of opinion from the members regarding their experiences with radium in these cases was requested.

DISCUSSION

It was generally agreed that radium gives splendid results in such cases—suberythema doses, not more often than once monthly.

POIKILODERMA. Presented by Dr. Lane.

M. R., an unmarried woman, presented an eruption which had started about six years previously. The eruption gradually spread, covering a large portion of the body almost symmetrically and presenting many different appearances, of which the most striking features were pigmentation, atrophy and minute hemorrhages. In many places the eruption presented a somewhat reticular arrangement. For a long time the eruption had been attended with moderate itching. A small, round, hard tumor, about one half inch (1.27 cm.) in diameter and elevated about 0.6 cm. was seen on the dorsum of the left foot. There was moderate scaling over the whole surface of the body. The diagnosis of poikiloderma was suggested, although in this case there was more scaling and less telangiectasia than had been seen in the cases previously presented before the Society. The possibility of mycosis fungoides was considered. Reports of various laboratory examinations have not been received.

DISCUSSION

DR. WILLIAMS: I wish that Dr. Lane would explain the presence of tumors and papules.

DR. LANE: I think that the tumors do not have any etiologic relation with the disease, but that they are a coincidence. The first case I observed showed a tumor formation. The tumors were probably Hodgkin's disease, though the pathologists would not make a positive diagnosis.

DR. WISE: It is difficult to make any other diagnosis from the patient's appearance. She will have to be examined more carefully and watched for a long time before a positive diagnosis of poikiloderma can be made.

DR. WHITEHOUSE: The cases all seem to have different features clinically. The little girl whom I showed, I saw again at New London this summer. The atrophy of the skin has extended to the muscles, and she is practically crippled and confined to her bed. The muscles are shriveling rapidly. In my other case, the patient does not present these features. The eruption in my cases resembled chronic roentgen-ray dermatitis. This is not true of Dr. Lane's case. The little girl I presented has lost all of her hair, and the roentgen-ray burn appearance of the skin behind the ear has now spread over the scalp.

DR. KINGSBURY: I suggest the possibility of mycosis fungoides.

DR. HIGHMAN: I think it would be advisable to make a roentgen-ray examination of the mediastinum in order to determine the presence of enlarged glands.

DR. MACKEE: It will be necessary to exclude the premycotic stage of granuloma fungoides, leukemia and other members of this group.

VERRUCOUS CRIBRIFORM NEVUS OF SCALP WITH POSSIBLE SARCOMA. Presented by Dr. Lane.

Miss J. M., a school teacher, aged 30, presented a nevus of the scalp on the right side of the head, extending from just in front of the ear to about the center of the top of the head, three and one half inches (8.89 cm.) long and one inch (2.54 cm.) wide. The area was hairless and the surface was covered with small yellowish nodules. In the center of the area were two small erosions which the patient said had been present for five or six years.

DR. MACKEE: The lesion looks to me like the remains of a nevus cerebelliformis which had been treated with solid carbon dioxide or some similar method. The area of ulceration is likely the beginning of a sarcoma. A nevus of this type is potentially dangerous. I have seen two patients treated with solid carbon dioxide in which fatal sarcoma developed several years subsequently. It seems advisable never to treat this particular type of nevus with any method which fails to destroy the lesion completely. In this case I recommend the complete excision of the entire nevus.

DR. WISE: I agree with Dr. MacKee. I saw the patient about three or four years ago and noted the ulcerated spots, which are probably due to irritation from a comb, and I have advised the patient to have surgical excision or removal by electrodesiccation, followed by skin grafts.

DR. HIGHMAN: I agree with Dr. MacKee and Dr. Wise in regard to the advisability of radical surgical excision; but, in connection with Dr. Wise's last statement, if this lesion was a verrucose nevus, electrodesiccation will not destroy it, for such lesions seem to have a tendency to return. There is a tendency to malignancy in all these lesions, particularly when tampered with. I think, as Dr. MacKee said, they are sarcomatous. Perhaps the best way to approach the case would be to excise a small piece for examination while the patient is under an anesthetic and then to proceed radically if there is any suggestion of malignancy.

ATYPICAL PITYRIASIS ROSEA. Presented by Dr. Fraser.

A girl, aged 14, presented a nonitching maculopapular eruption of two months' duration. With the exception of a few scattered lesions on the face, the distribu-

tion was confined to the trunk and limbs. There were no mucous membrane lesions, and the scalp, palms and soles were free from the eruption. Evidence of generalized adenopathy was not present; there was no history of an initial lesion, nor were there constitutional symptoms at any time. When the patient was examined two weeks before presentation, the case bore a strong resemblance to a secondary syphiloderm. When presented, the lesions were fading and the resemblance was less. The Wassermann reaction was negative. The histologic study of sections did not support the diagnosis of syphilis.

DR. KINGSBURY: From the appearance of some of the lesions, especially those on the forehead, it would seem that a diagnosis of beginning psoriasis might be considered as a possible alternative to pityriasis rosea.

DR. FRASER: I am not in favor of the suggestion that this may be a case of psoriasis; the distribution of the lesions and their arrangement (many of them along the lines of cleavage) and the absence of features such as the bright red color, powdery scaling and bleeding puncta, is against that diagnosis. The eruption is now beginning to fade, and this is what one would expect in a self-limited disease. Furthermore, the microscopic observations favor the diagnosis of pityriasis rosea. Vesicles, which are frequently seen in pityriasis rosea but seldom, if ever, in psoriasis, are present in the sections. I believe the case should be recorded as an atypical maculopapular type of pityriasis rosea.

PSORIASIS TREATED WITH A SPECIFIC VACCINE (THREE CASES). Presented by DR. CLARK.

In December, at the Atlantic Conference, Miss Mary A. Marcus, of Boston, made a report on the recovery of an *actinomyces*-like organism from psoriatic lesions. (ARCH. DERMAT. & SYPH. **13**:712 (May) 1926.) This summer, Miss Marcus came to my clinic at the Post-Graduate Hospital and asked for an opportunity to use a specific vaccine in cases of psoriasis. She started in July and had been working ever since on psoriasis. The three patients shown were selected for presentation as they seemed to characterize the progress made under this treatment. They had been receiving inoculations with living organisms, scarifications and injection of vaccine.

Miss Marcus claimed to have produced psoriasis in a person who had never had the disease, and she had recovered the organism from the lesions thus produced. Typical psoriasis lesions seemed to develop in psoriatic patients at the site of inoculation unless the patient was given the vaccine at the same time, under which condition the typical lesion did not develop. It had been noticed that psoriatic patients had a musty odor, and the cultures had exactly the same odor. One intelligent patient claimed that since he had been taking the treatment he had not noticed the musty odor about his person.

CASE 1.—H. A. B., a man, aged 31, born in the United States, a bacteriologist, came under observation two years ago with scattered lesions of inveterate type. For a year and a half this patient was treated with many internal remedies, a protein-free diet and local stimulating ointments of tar, salicylic acid, white precipitate and chrysarobin—all with little or only temporary improvement. For several months the patient gave himself injections of an autogenous staphylococcus vaccine made from the superficial part of his own lesions. He also received a course of sodium thiosulphate.

Three months before presentation he was transferred to my clinic at the Post-Graduate Medical School and Hospital, and there began to receive specific vaccine made from cultures of an *actinomyces*-like organism recovered from psoriasis lesions by Miss Marcus. After the first month, the patient began to improve.

Most of the large thick lesions had thinned considerably and paled, and some of them had disappeared without any local or other type of treatment. The patient himself was enthusiastic about the progress he had made, which seemed to him more definite than anything that had previously been done in his case. He said that he himself had been able to recover from his own lesions the *actinomyces*-like organism. He certainly seemed to show a considerable improvement under this treatment after three months.

CASE 2.—C. S., a woman, aged 31, a book-keeper developed psoriasis about eighteen months previously. A photograph taken before the treatment was presented showed there had been a distinct improvement. The patient was enthusiastic about the treatment. She had not had any other local or general treatment nor any modification in the diet; only the vaccines and inoculations by Miss Marcus.

CASE 3.—H. L., a man, aged 65, born in the United States, retired, had had a severe psoriasis for three years. The patient said that a long course of arsenical treatment at the early stage of the disease had seemed temporarily to improve the condition, but that it soon recurred and was much worse than before. The specific treatment was begun three months prior to presentation. After the first month he began to show a gradual, steady resolution of all the lesions, with absolute clearing up of the larger ones. The patient had not had any other local or internal treatment nor any modification of the diet. This patient also was enthusiastic about the results of treatment.

DISCUSSION

DR. MACKEE: We should be careful not to assume too much as a result of therapy in this disease. Psoriasis behaves differently in various persons. The possibility of spontaneous improvement must always be kept in mind. Not infrequently a psoriatic eruption will improve or disappear as a result of foreign proteins—such, for instance, as antityphoid vaccine, furunculosis vaccine, milk, pollens and other kinds. There have been articles written in the past by physicians who used foreign proteins in cases of psoriasis, with good results. In this instance, we are told that the causative organism has been found and that a specific vaccine has been developed, which is a remarkable scientific discovery and of great therapeutic value if it proves to be true. It will be necessary to have a large amount of therapeutic material and indisputable evidence of the transmission of the disease to a large number of persons who never had psoriasis, before framing a final opinion.

DR. HIGHMAN: I reflect Dr. MacKee's scepticism about this, and for the reasons mentioned. I think we should keep an open mind with regard to Miss Marcus' work, and most guardedly accept her observations and conclusions.

DR. FRASER: I agree with Dr. MacKee and Dr. Highman. I am not convinced that psoriasis has been reproduced. Was this organism demonstrated in the epiderm or corium?

DR. CLARK: Miss Marcus recovered the organism from the deep tissue.

DR. LANE: It seems to me that these organisms and cultures should be submitted as soon as possible for study by an independent, disinterested bacteriologist and mycologist.

DR. CLARK: I am in accord with everything that Dr. MacKee and Dr. Highman have said. I have been as sceptical as they, and am still so. I brought the cases here because I am so sceptical, and I propose to bring others, if I am permitted, and let the members see these clinical results and try to decide whether or not the method has therapeutic value.

PARAPSORIASIS EN PLAQUES. Presented by DR. WISE.

E. D., a man, aged 69, presented a well developed case of parapsoriasis in patches, of four year's duration. These patients usually failed to show improvement under roentgen-ray treatment, but this one had been treated on one side with roentgen rays, and the other side had been left alone. The treated side showed marked improvement. The lesions consisted of slightly scaly, reddish-brown, sharply marginated oval areas, from 1 to 6 inches (2.54 cm. to 15.24 cm.) in their long diameters, situated on the upper and lower extremities and the lumbar region, and a few on the abdomen.

PARAPSORIASIS. Presented by DR. SCHWARTZ.

F. B., a man, aged 49, presented an eruption with a duration of fifteen years. The lesions were principally on the trunk and limbs, and consisted of well defined, reddish-brown, noninfiltrated patches of various sizes and shapes. In addition, there were a few distinct papules over the extensor surfaces of the elbows showing the clinical characteristics of xanthoma tuberosum. The blood chemistry was normal. The urine was negative. Microscopic examination of a section from a noninfiltrated area showed a histologic picture which conformed to the diagnosis of parapsoriasis.

DISCUSSION ON PSORIASIS

DR. MACKEE: The patient presented by Dr. Wise improved under roentgen-ray treatment. It has been fairly well demonstrated that parapsoriasis does not respond to such treatment. Of course, it must not be assumed that an occasional case might not be favorably influenced by the roentgen ray. However, when an eruption of apparent parapsoriasis has not been histologically studied and it has responded favorably to roentgen irradiation, there is at least ground to suspect the possibility of mycosis fungoides.

DR. WISE: I agree with Dr. MacKee.

A CASE FOR DIAGNOSIS (PYRODERMA?). Presented by DR. SCHWARTZ.

J. L. J., a boy, aged 17 months, had a history suggestive of infantile eczema of the face, occurring at varying intervals since the age of 2 months. When presented, there was an extensive, deep-seated, ulcerating area on the forehead and right side of the nose. There was marked scarring on the cheeks and chin—the result of previous lesions. The child was below weight and its general condition was poor. The hemoglobin content of the blood was 62 per cent. The hands and feet were cold and cyanotic and the nails showed atrophic changes. Since admission to the hospital, the child had run an irregular temperature, varying from 98 to 103.6 F. The Wassermann reaction and the blood culture were negative. A smear from the facial lesions showed a gram-positive extracellular diplococcus (encapsulated).

DISCUSSION

DR. HIGHMAN: In my opinion, it is an ordinary impetiginous eczema in a peculiarly susceptible person.

DR. WILLIAMS: One point to add to Dr. Highman's remark is the possibility of some toxin acting on the nervous system and making the skin susceptible. The child's extremities are cold, and the bandlike distribution on the right cheek and forehead is much like a zoster; it would seem that there might be some connection between an improper functioning of the nerves and this condition. In connection with what Dr. Highman said about increased susceptibility, I recall a man who has had repeated attacks of erysipelas whose son is having boils all the

time; he had had a double mastoid operation, and the scars of the mastoid broke down a year later. The father and son did not seem to have any resistance to the organisms of suppuration.

DR. HIGHMAN: I recall the case of a well known physician who is susceptible to repeated attacks of sinus infection and who almost lost his life in one of these attacks. His children have recurrent attacks of mastoiditis. In connection with what Dr. Williams has just said about family susceptibility, I think this is an important point to bear in mind.

DR. BECHET: I think that both Dr. Highman and Dr. Williams have a correct view of the case. There is, however, a close relationship between the endocrine system and the sympathetic nerves. The child shows definite evidence of endocrine deficiency, and this deficiency may possibly have some rôle in the causation of the lowered resistance to infection.

DR. MACKEE: I agree with Dr. Highman in regarding it as a pyoderma in a child who has exceedingly poor health. We all see patients with a low general or specific resistance, in whom the pyogenic organisms cause unusual eruptions. I have such a patient now who is literally covered with boils. Acne cachecticform, with which you are all familiar, is possibly an example of low specific resistance to pyogenic organisms.

DR. LANE: I do not see how we can say that there is any endocrine disturbance in a patient so young, especially when we do not have any evidence of it.

DR. SCHWARTZ: I saw the patient last week at the Englewood Hospital, and the lesions were all covered with scarlet-red ointment so that it was difficult to make a definite diagnosis. The nature of the condition is evident. I agree with the conception of the case as expressed by Dr. Highman, and I think that it is a severe form of pyoderma due to the patient's underlying low resistance. One week ago the child was given a transfusion of 150 cc. of blood, and since then the lesions have distinctly improved; the temperature has been varying between 98 and 100 F., whereas before it was 103.5 F. The general condition is much better.

LUPUS ERYTHEMATOSUS TREATED WITH GOLD. Presented by DR. CLARK.

C. C., a housewife, aged 40, born in the United States, presented herself for treatment two years previously, with a discord lupus erythematosus of the greater part of the nose and of the middle three fourths of the upper lip. Since that time, various types of treatment, including the use of iodide of iron and various glandular extracts internally, had failed to cause any considerable improvement; externally, the following treatment had been used: painting with phenol (one part) and lactic acid (4 parts), strong lotio alba and various ointments.

Two weeks before presentation, this patient was given 100 mg. of gold thiosulphate intravenously, and since then had received 100 mg. three times a week, together with one-tenth of a grain (0.006 Gm.) of gold chloride by mouth three times daily, after the method outlined by Dr. Schamberg. Six injections had been given. The lesions were markedly improved, and the long-standing subjective symptoms of tingling and burning had disappeared.

URTICARIA PIGMENTOSA. Presented by DR. MACKEE.

Mr. C. K., a private patient, aged 31, had an eruption on the abdomen which was first noted five years previously. Within a few months, it had spread over the trunk and arms, but had not spread much since then. The eruption consisted of brown macules the size of split peas, which would quickly change to

wheals when rubbed. At times there was considerable itching, and occasional dermographism was conspicuous. The patient was born in America, and had always enjoyed the best of health. The stool and urine were negative, as were also the blood chemistry and the Wassermann reaction.

URTICARIA PIGMENTOSA. Presented by DR. WISE for DR. ELLER.

W. M., a boy, aged 7, presented an eruption which consisted of numerous macular purpura-like lesions which were scattered over the trunk and arms and especially on the back. The eruption had been present six months and itched slightly. Rubbing one of the lesions would cause a wheal to appear. A blood count, on November 16, showed: red blood cells, 4,500,000; white blood cells, 10,000; hemoglobin, 93 per cent; differential count, normal. The patient was apparently healthy otherwise.

DISCUSSION

DR. LANE: I agree with the diagnosis.

DR. WILLIAMS: I rubbed the skin of the child and could not get any elevation; the discoloration, instead of being a uniform brown as one would expect, was somewhat reticulated, and more the color of a resolving hemorrhage. I would say that the child has purpura and that many of the lesions are resolving.

DR. FRASER: The only way to settle the question is by microscopic examination. There are three cardinal features in the histologic picture of urticaria pigmentosa—mast cells, pigmentation and fraying of the elastic tissue. A case without mast cells should not be called urticaria pigmentosa.

DR. HIGHMAN: Although purely a laboratory matter, Dr. Fraser's remarks cannot go unchallenged. The mast cells are characteristic of urticaria pigmentosa when they are present; but their absence does not rule out the disease. They are present at the fastigium of the lesion and may be absent, and are usually only sparse during the evolution and involution of the lesion—an obvious phenomenon when it is recalled that the lesions must have an origin and finally disappear. Hartzell pointed out all this a decade ago, and it is a testimony to the inertia of dermatologists that this simple fact is not yet recognized.

DR. WISE: Only a little while ago I reported the case of a patient with urticaria pigmentosa in which mast cells were not found at the first biopsy; a second biopsy showed mast cells a few weeks later.

LUPUS VULGARIS. Presented by DR. KINGSBURY.

G. B., a man, aged 40, born in the United States, said that the first lesions of the disease had occurred on the face when he was about 10 years of age. When presented, he had extensive patches of lupus vulgaris, palm size and larger, on the shoulders, elbows and flexor surface of the forearms, as well as on the buttocks, with smaller sized lesions on the thighs and legs. All the lesions on the body were covered with thick, silvery scales, but when removed the characteristic lesions of lupus vulgaris were apparent. There were large sized patches on the forehead, cheeks and neck, with considerable scarring. On the left cheek was an ulcerating area with granulations nearly an inch (2.5 cm.) high. Biopsy did not show any evidence of malignancy.

RUPIAL SYPHILID. Presented by DR. KINGSBURY.

J. D., a truck driver, aged 28, first came under observation five months prior to presentation, when he had an initial and secondary lesion. He received

one injection of arsphenamine, but did not report again until one week before presentation. He then presented on the forehead, upper lip, back and arms, large rupial lesions.

DISCUSSION

DR. WHITEHOUSE: We do not see these cases often now. Years ago, we used to have many cases of rupial syphilid; they depend, not on the virulence of the infection, but on the greatly reduced state of the general health, and, of course, inadequate treatment.

A CASE FOR DIAGNOSIS (COLLOID DEGENERATION?). Presented by DR. WISE.

Mr. B. S., aged 45, referred by Dr. Pels of Baltimore, presented himself because he had an eruption on the upper part of the chest, the neck and shoulders, front and back. His past history was not of any importance, except that he was being treated by a gastro-enterologist for "gas on the stomach," and he had had boils several years before. The eruption began as "pimples" on the chest eight years before presentation. Others appeared, eventually leaving white areas as seen on presentation. These had increased in number, spreading over the shoulders and on the upper part of the back. There were not any subjective symptoms, and the only treatment was washing with alcohol. Results of his general physical examination were negative with the exception of finding postoperative adhesions in the upper and lower right quadrant. Psychoneurosis was 3 plus. The stomach was in an irritable condition.

His physical condition was excellent. The epitrochlear and axillary glands were easily felt. There was a lasting and urticarial dermographism. On the right side of the chest, in the region of the clavicle and extending from the sternum toward the right shoulder and also on the neck and as far as the spine, were grouped lesions which had two characteristics. There were subepidermal nodules, slightly inflamed, which were best seen on the neck and on the posterior portion of the trunk, having a dull white color tinged with pink and suggestive of cysts. They varied in size up to 1 cm. in diameter. Where they were grouped, they were suggestively circinate in arrangement. The skin over them was normal in most instances, and the nodules, on palpation, were deeply set, freely movable but attached to the upper layers of the skin. These nodules were not painful on palpation. Another condition noted was that of patches of pink inflammatory reaction, when viewed with the lens appearing as slightly defined papules located over the areas just described. They were round and polygonal, flat, and some of them were crusted, giving an impression of slight trauma as if from scratching. On the left side of the back, just beyond the midline, there was a linear eruption composed of flat, shiny, waxy, tiny papules, both grouped and confluent, superficially located, just palpable, and of a buff pink, without umbilication, yet suggesting lichen planus.

A specimen taken from back of the shoulder showed a normal epidermis. There was no noticeable change in the papillary layer. There appeared to be an increase in the thickness of the corium. There was considerable edema and spreading of tissues. There seemed to be, further, a rather poor staining quality to this part of the section. There was no fibrin formation. However, a number of large wide spaces were present in line with the epithelium, which might have been the space occupied by lymphatics. The elastic tissue fibers appeared swollen. Around the vessels, which were normal, there was an occasional area of slight infiltration of small round cells.

Correlated with the clinical appearance one would think first of a colloid degeneration, but the variation from the normal in the corium was not sufficiently striking to warrant this diagnosis.

BROMODERMA. Presented by DR. BECHET.

R. F., a girl, aged 13, was brought by her mother to Dr. Aitkin's service suffering from an eruption of the face and legs, of four months' standing. She had several large papulopustular lesions on the face, and both lower legs were covered with condylomaform patches, from which exuded seropus. She had been an epileptic for eleven years, having from ten to fourteen attacks a year, and had taken bromide at intervals for several years. For the previous six months she had been taking bromide steadily. The case was presented because the patient showed two types of the eruption, the papulopustular and the condylomaform; and because it was the presenter's intention to treat the patient with decinormal salt solution intravenously administered, and then exhibit the patient at a later meeting in order to show the rapid resolution of the lesions almost invariably observed after the use of this method, as advocated by Wile. Experience had shown that nothing else gave as good results as this method of treatment, particularly in the fungating condylomaform type.

A CASE FOR DIAGNOSIS (DERMATOPHYTOSIS?). Presented by DR. FRASER.

A woman presented an apparent fungoid infection, probably dermatophytoses, from which she had suffered for nine years. She had improved considerably under treatment with Whitfield's ointment and chrysarobin.

The eruption consisted of inflammatory patches made up of papules and papulopustules. It involved the whole genitocrural region and extended over the genital organs and public area to the lower surface of the breasts. The hands and feet were also involved.

DISCUSSION

DR. WILLIAMS: This is a most interesting case, but I would never present it as a case of dermaphytophytosis unless the organism was demonstrated. Much harm has been done by the presentation of such unverified cases, as these presentations build up a conception of the symptomatology of dermatophytosis which is utterly without foundation. The symptomatology of the foot cases is fairly well established, as the organism is frequently found on the feet. The symptomatology of the hand cases is not established, as the organism is seldom demonstrated on the hands. The discovery of mycelia in foot lesions when the hands of the same patient present somewhat similar lesions is suggestive, but not conclusive. To argue that a given symptom is caused by a mycotic organism because it improves under treatment with Whitfield's ointment is puerile, when we remember that many cases which are proved by the microscope to be trichophytosis are absolutely resistant to Whitfield's ointment.

DR. HIGHMAN: I agree with Dr. Williams that the term should not be used unless the epidermophyton is found. Similar infections caused by other strains should be called dermatophytosis.

DR. FRASER: What I said was that this was probably an epidermophyton infection. Dr. Williams criticism is correct. A diagnosis should not be made in these cases without demonstrating the organism. I shall endeavor to do this and report the observations at a future meeting.

A CASE FOR DIAGNOSIS (MULTIPLE ANGIOMA?). Presented by DR. FRASER.

M. F., a woman, aged 40, was admitted to the Cornell Clinic on Aug. 11, 1926, complaining of slowly spreading varicose veins or angioma of the right arm. She said that when she was 6 weeks old she had had some groups of dilated blood vessels on the dorsum of the right hand; by the time she was 25 years old this

group of vessels had extended along the surface of the arm to the elbow. As presented, the process had extended to the shoulder. Four operations were performed on the arm between 1908 and 1915. Three of these were performed in a clinic by Dr. John B. Murphy in Chicago; the last was performed in the Mayo Clinic in 1917. The operations consisted in removing groups of dilated blood vessels. A report from the Mayo Clinic stated that groups of varicose veins about the right hand were removed in 1917. She had two intravenous injections of gelatin between 1921 and 1923, which were given by some physician who thought they would increase the coagulation of the blood. The patient believed that the operations had helped the function of the arm considerably. She still suffered from occasional numbness of the fingers at night with, occasionally, slight tingling. She could use the hand in a normal way.

The patient was a poorly nourished woman, with multiple bluish discolored areas of vascular nature over the right upper extremity, from the dorsum of the hand to the axilla and shoulder. There were numerous longitudinal scars over the whole extremity.

Blood examination showed: red blood cells, 3,480,000; polymorphonuclears, 41 per cent; lymphocytes 59 per cent. The coagulation time was three minutes; the Wassermann reaction was negative. Roentgen-ray examination of the arm showed deposits of density, indicating calcium in the soft parts of the arm, about fifteen or twenty of these being scattered around.

The case had been shown to Dr. Ewing, who said that he had never seen one like it. He believed the condition to be a slowly developing angioma and advised roentgen-ray therapy with low voltage radiation.

DISCUSSION

DR. WILLIAMS: The appearance of these lesions is like that of the lesions in a small child who has angioma. We know that angiomas occurring in infants have a way of spreading for an indefinite period, but this spreading usually stops at the end of a few months—we do not know why. This case appears clinically as though the impulse to stop had not occurred, and whatever makes it progress in a child is still active. I should think the best treatment would be the treatment for angioma—treating the spreading portion with radium.

DR. MACKEE: I agree with Dr. Williams' diagnosis, namely, cavernous angioma. The unusual feature of this case is that it began in infancy, has covered a large area, and is still evolving. Radium and the roentgen ray are not of much value in cavernous angioma that has existed for many years and that has ceased to develop. In this instance, however, the lesion is still progressive, and it is possible that radium or roentgen rays would be successful. The explanation is that angiomas respond well to irradiation because the neoplasms are composed of rapidly developing blood vessels, which means rapidly dividing cells, or embryonic tissue. Such tissue is amenable to the inhibitory action of irradiation. After the tumor has ceased to grow and has become fixed such treatment ceases to be effective.

The suggestion was made to treat this patient with low voltage roentgen rays I would advise just the opposite—not less than 150,000 volts, or an approximate 9 inch spark gap with at least 3 mm. aluminum filtration. I think the effect would be even better with a voltage of 200,000 or 250,000 and a filter consisting of 0.5 mm. copper and 1 mm. aluminum. In this particular case, in which the lesions are so deep, I would advise against the beta rays of radium. If radium is used, one should depend on the gamma rays, filtering with 0.5 mm. silver

and 1 mm. brass, and the radium should be placed at a distance of at least half an inch. It would be advisable to give suberythema doses.

DR. WHITEHOUSE: My conception of the case is that the condition is advanced congenital cavernous nevus.

XANTHOMA TUBEROSUM MULTIPLEX. Presented by DR. WILLIAMS.

David L., aged 20, born in Russia, presented a condition which began in January, 1926, on the forehead near the hair line, then on the right side of the neck, and then spread over the face, trunk and proximal segments of the extremities. When the patient was exhibited, most of the lesions were on the face, neck and trunk, with a few on the forearms and lower thighs. The general health remained the same.

The earliest lesion was a small dull red, rounded papule arising from the normal skin; the largest lesions were about 3.17 mm. in diameter and were yellowish red. The red color of the smaller lesions disappeared when the skin was stretched, revealing a yellow color in all of them. There were also pale brown stains, the site of former lesions. The blood sugar content was 60 mg.

The pathologic report showed that under the epidermis there was an infiltration of large connective tissue cells and numerous foreign body giant cells. There were a few clear staining cells that suggest cholesterol deposits.

DISCUSSION

DR. MACKEE: It is one of the most remarkable cases of xanthoma that I have ever seen. Clinically, the case resembles xanthoma diabeticorum rather than xanthoma tuberosum multiplex. The lesions are reddish yellow rather than yellow; they are numerous and small; some of them are smaller than the head of a small pin. There are numerous lesions on the face, and the sites of predilection for xanthoma tuberosum multiplex are rather free from lesions. Many of the papules are flat-topped, shiny, and suggest lichen planus. Another unusual feature is the fact that the lesions disappeared under roentgen-ray therapy. This can possibly be explained because the lesions are young and growing rapidly. This provides tissue of embryonic type, which is likely to feel the inhibitory effect of the roentgen ray.

MILIUM. Presented by DR. FRASER.

The patient came from the service of Dr. Schwartz at the Cornell Clinic, and was first seen on June 8, when he complained of severe chronic itching of the face. He was given nine one-fourth skin unit doses of roentgen rays. During the time he was receiving this treatment, the eruption, which consisted of smooth, whitish, pearly papules, suddenly appeared on the upper part of the face. Microscopic examination of sections showed the histologic picture of milium.

DISCUSSION

DR. MACKEE: I could not detect any milia. There was a large number of follicular papules, each one of which contained a dark follicular plug. From a clinical standpoint, I would consider the case one of acne papulosa or, perhaps, tiny sebaceous cysts.

DR. WISE: I will go a step further and say that the man probably had the lesions before the roentgen-ray treatment was given, and had not noticed them; and the roentgen-ray therapy made him look in the mirror and discover the lesions. I think they are sebaceous cysts, such as one would see in a young man's acne.

DR. FRASER: I saw the man before treatment, and his face was perfectly smooth. There are no comedones in these lesions, and the histologic picture is not that of acne vulgaris.

LUPUS FOLLICULARIS. Presented by DR. FRASER.

The patient, a young woman from the Cornell Clinic, had suffered from an eruption for seven months, which consisted of pin-point and millet-seed-sized papules, mostly discrete but a few aggregated. Some of the lesions were capped with a pustule while others presented a smooth, reddish, glistening surface with a central depression. Where the lesions had undergone resolution, varioliform scars remained. Microscopic examination of sections showed replacement of hair follicles by epitheliod and giant cells of the foreign body type concentrically and radially arranged around a necrotic center. The case was presented as an example of the disseminated follicular lupus of Tillbury Fox.

ST. LOUIS DERMATOLOGICAL SOCIETY

Regular Meeting, December, 1926

ROBERT H. DAVIS, M.D., *President*

A CASE FOR DIAGNOSIS. Presented by DR. E. R. SEALE. (From the Barnard Free Skin and Cancer Hospital, service of Drs. M. F. Engman and W. H. Mook.)

M. J., a white girl, aged 17, presented a lesion on the left leg of four years' duration, during which time it had become ulcerated, with subsequent healing. It had undergone this process several times. There were no subjective symptoms. Examination revealed an elevated lesion about 2 cm. in diameter on the medial surface of the left leg immediately above the ankle. The lesion was deep purple except the central portion, which was lighter, thickened, and dotted with minute crusts. There was slight induration of the lesion. The inguinal glands were not enlarged.

DISCUSSION

DR. ZWICK (Cincinnati): Without a definite history of tuberculosis or a laboratory report, I would attempt only a tentative diagnosis of tuberculid.

DR. TOBIAS: There is evidence in this case of poor peripheral circulation. My diagnosis would also be tuberculid.

DR. SEALE: It was impossible to obtain a history of tuberculosis in the patient or from any of her relatives. In the clinic we made a diagnosis of erythema induratum.

DR. LANE: There was no family history of tuberculosis. The patient's parents are both living in Italy, and are apparently in good health. The diagnosis lies between erythema induratum and sarcoid nodularis which closely resembles erythema induratum.

DR. DAVIS: I also thought of a diagnosis of sarcoid. I do not believe, however, that a differential diagnosis between sarcoid and erythema induratum or another tuberculid can be made without a section and a laboratory report.

DR. ZWICK: With all due reservation I would register my impression that the lesion is of the Darier-Roussey type. In regard to the significance of the family history, one should bear in mind that this is sometimes rather deceptive. As a case in point I might mention that I have a patient under my care at this time without any history of tuberculosis in the family. Her case was diagnosed elsewhere by an experienced observer as an "érythème induré de Bazin." I confirmed the clinical diagnosis and the etiology was supported by a local tuberculin test. Only after long acquaintance with the patient did I learn that in her youth she had waited on a woman who had an active pulmonary tuberculosis and coughed a great deal. In her ministrations my patient came in close contact with this bacilliparous woman. The family history alone does not exclude a source of infection.

A CASE FOR DIAGNOSIS. Presented by DR. E. R. SEALE. (From the Barnard Hospital, service of Drs. M. F. Engman and W. H. Mook.)

C. E., a white man, aged 23, gave a history of lesions of six months' duration on the tongue, involving the tip, the dorsal central portion and the right anterior edge. The patient said that they had begun as small white spots which coalesced, forming a large lesion, the latter disappearing in a few days. The only subjective symptom was a slight burning sensation on eating spicy foods. Examination revealed only one lesion on the right anterior edge of the tongue. It was oval, 4 cm. in length, and involved the right edge of the dorsal surface, extending down to the base. It was sharply defined and was denuded of surface epithelium. There was no induration. The papillae in this area, as well as those on the tip, were bright red. The patient was under treatment for pulmonary tuberculosis.

DISCUSSION

DR. LANE: The fact that the lesions appeared on different portions of the tongue, involving chiefly the tip and the dorsal surface, their healing spontaneously, together with the slight subjective symptoms, the redness and slightly depressed borders, lead me to believe that the condition is a transitory, benign plaque of the tongue.

DR. SEALE: The present lesion is entirely new. The one observed a week ago, which was about the size of a half dollar, has healed, and an entirely new lesion has appeared at the same site.

DR. CONRAD: When I first observed the patient I thought the disease was Moeller's glossitis, but at this time that can be ruled out, as I cannot now see characteristics of Moeller's glossitis, and it is now giving evidence of transitory benign plaques of the tongue.

DR. DAVIS: The lesions suggest geographic tongue, although there is deeper involvement than is ordinarily seen in geographic tongue. It would be of interest to know, as the patient has active tuberculosis, whether or not this might modify the appearance of an ordinary geographic tongue.

DR. CONRAD: I have a patient with the same condition without any history of tuberculosis. The lesions appear, then disappear, without any apparent cause.

A CASE FOR DIAGNOSIS. Presented by DR. I. H. NEECE (Decatur, Ill.).

W. R., aged 56, a farmer, had been suffering for the last four or five years from a pruritic condition of the skin over the flexor surfaces of the elbows, knees and ankles. The condition, which was confined to those areas,

lasted during the winter and usually disappeared during the summer months. In October, 1925, the patient had a recurrence at the old site, with a gradual extension over the extremities and the entire body. He was given various lotions, ointments and roentgen-ray treatment, with the result that the condition became generalized. When first seen by Dr. Neece in May, 1926, the lesions were characterized by marked redness and a generalized erythema with thickening of the skin and fissure formation. Desquamation was characterized by fine, then coarse, scales which easily peeled off. They readily formed again and were constantly being shed, so that large handfuls could be collected. When the scales were removed, the underlying surfaces were red, glossy and dry. At times the surfaces became moist, more markedly on the limbs than on the body. Following the period of desquamation, multiple abscesses developed in the axillae, groins, flexor surfaces of the leg, and at various places on the body, usually occurring at the points at which the pruritus was most intense. At presentation the body was comparatively free from eruption, except the lower extremities and the hips, which showed certain lichenoid areas.

DISCUSSION

DR. BROCKELMANN: I believe that the present condition is a dermatitis caused by various local applications. The underlying cause is probably senile pruritus.

DR. ZWICK: To me it appears to be a "winter" dermatitis in which pruritus is often confined to the lower limbs. It seems rather early in life for a senile pruritus. However, one might have to take into account the possibility of exposure and sensitization to pollen and dust in his occupation as a farmer. I am inclined to consider that the acute stage first observed was a dermatitis caused by some external remedy used. The present condition looks like a receding generalized dermatitis.

DR. NEECE: The patient has received no treatment since June, except sunbaths.

DR. TOBIAS: I think the so-called "winter pruritus" is responsible for the fine follicular lesions caused by scratching and irritation. I think the condition which the patient had a year ago, when there was a generalized lichenification, was due to generalized dermatitis exfoliativa from too vigorous local applications.

DR. CONRAD: I agree with Dr. Tobias' opinion. As for the abscess formation, this could be accounted for by secondary infection.

DR. NEECE: For the further information of those present, there is a prostatic condition present which has not heretofore been mentioned. The man has a four plus prostatitis, for which he has refused treatment. Could there be any relation between this condition and the dermatitis?

DR. DAVIS: I do not think there is any interrelation except possibly for the factor of lowered resistance which would make the patient more susceptible to an inflammatory disturbance.

DR. ZWICK: Has the patient used any internal medication, for instance, methenamine? A perigenital pruritus frequently stands in relation to a prostatitis and cystitis.

DR. NEECE: The patient has used no internal medication.

DR. TOBIAS: Is the condition a simple hypertrophy or an inflammatory condition?

DR. DAVIS: Prostatitis might be a factor, but it probably is not the exciting cause.

BLASTOMYCOSIS. Presented by DR. E. R. SEALE. (From the Barnard Free Skin and Cancer Hospital, service of Drs. M. F. Engman and W. H. Mook.)

J. M., a white man, aged 74, had been presented at the November meeting. The consensus of opinion at that time favored a diagnosis of blastomycosis, although blastomycetes could not be found. Since that meeting many smears and cultures had been made without avail. Microscopic section also was made. Blastomycetes were not found, although otherwise the sections were fairly typical. The patient improved on potassium iodide medication.

DISCUSSION

DR. CONRAD: From the condition of the skin alone it would be difficult to make a positive diagnosis of blastomycosis. The microscopic section, although it has to a great extent the appearance of blastomycosis, is not typical.

DR. TOBIAS: It is strange that the organisms could not be found in lesions of so extensive a type. Why not inject some of the tissue into susceptible animals?

DR. ZWICK: I was going to suggest animal experimentation. In addition I should like to see tests on the skin, analogous to a Pirquet test, with material from cultures of known organisms, such as *Sporotrichum* and *Blastomyces*.

DR. SEALE: We made several cultures, but have found only *Staphylococcus*.

DR. ZWICK: My idea is not only to make cultures from the patient's lesions, but to prepare antigens (extracts) from cultures of various identified fungi; *Blastomyces, Oidiomyces* and others for cutaneous tests. Occasionally such tests serve a useful diagnostic purpose and at least help to determine the group to which the etiologic organism belongs.

MULTIPLE ANGIOMAS: CASE SHOWING RESULTS OF THERAPY. (Presented from the Barnard Free Skin and Cancer Hospital, service of Drs. M. F. Engman and W. H. Mook.)

An infant, aged 3 months, had previously been presented before the St. Louis Dermatological Society because of a history of congenital multiple nevi, totaling more than 800 over all parts of the body. The child was again presented to demonstrate the effects of therapy. In September, 25 mg. of radium, filtered with 0.4 mm. of lead, 1 mm. of silver, and thin rubber in two 12.5 mg. needles at 0.5 cm. distance, were applied to two lesions, one on the left cheek, the other on the left costal margin. Both lesions at this time were gradually fading, although the one on the trunk showed little more change than some adjacent untreated lesions. During a few months, more than 200 nevi on the upper extremities, as well as many on the face, scalp and neck, were treated for from 10 to 30 seconds with carbon dioxide. No instance of failure was noted, although occasionally the application had to be repeated. The dosage depended on the size of the lesion. It was found that application for 30 seconds produced vesicles in from twenty-four to forty-eight hours, which healed without treatment and did not leave scars. In some areas brownish stains which gradually faded were the only evidence of lesions successfully treated, which usually disappeared in two or three weeks. The point of interest in this case was the gradual decrease in size and color of practically all of the untreated lesions on the trunk.

DISCUSSION

DR. DAVIS: I should make the diagnosis of disseminated vascular nevi which have improved remarkably under treatment with carbon dioxide.

DR. BROWN: I agree with Dr. Davis.

DR. TOBIAS: The rarity of such a case in medical literature makes this one of special interest.

DR. BROCKELMANN: I question the wisdom of instituting treatment in so young a child.

DR. CONRAD: I felt that immediate treatment was indicated, in view of the remarkable results obtained.

DR. MOOK: I do not believe that the case belongs to the class of angiomas in the sense of nevi of the "bodkin" type, but that infants are sometimes born with telangiectases, which, instead of being angiomas in the sense of nevi, develop as telangiectasia. Occasionally similar lesions are seen on the face in adults, and lesions that are almost papular in the center. In other words, there is one central vesicle that leads up to and develops in spider-like growths. I have used electrolysis for this condition, the electric needle being inserted vertically into the center of each lesion, tapping the main vessel, after which the lesser ones disappeared. In the matter of deferring treatment, I agree with Dr. Brockelmann. I should prefer to wait until the child is old enough to apply electrolysis. There were instances in Dr. Engman's practice some years ago in which young girls developed telangiectases associated with hyperthyroidism. Sometimes these lesions disappeared, sometimes they remained. I think that the present case is interesting from the standpoint of the patient's general condition and in the effort to determine some systemic cause for the telangiectases.

MULTIPLE SUBCUTANEOUS LIPOMAS. Presented by DR. NORMAN TOBIAS.

B. K., a white man, aged 27, gave a negative history, saying that his present trouble began at the age of 12. The disfiguring subcutaneous growths began to appear first on the left forearm and then in other locations in rapid succession, new lesions forming from time to time. None of the growths were painful, although those on the forearms occasioned some discomfort because of irritation from the clothing. The patient had never been treated for this condition, but because of his abnormally increasing weight two years ago he received thyroid medication for a period of eight months. His weight chart is of interest: Ten years ago he weighed 145 pounds (65.8 Kg.); five years ago he weighed 165 pounds (74.8 Kg.); three and one-half years ago he underwent a tonsillectomy, after which his weight increased, as observed at present, to 218 pounds (98 Kg.).

Results of the general physical examination were essentially negative except for a pituitary type of obesity. Roentgenograms of the sella turcica were not available. Urinalysis was negative. At presentation numerous subcutaneous tumors arranged in rough symmetry involved the forearms and thighs particularly. There were also a few growths on the buttocks, abdomen and back. On the forearms there was a suggestion of linear distribution, although the lesions did not follow the distribution of the nerves. The tumors varied in size from that of a cherry to that of a plum, were fairly movable under the skin and not hard. Some of the growths were lobulated. The skin over the lesions on the forearms was red from friction of the adjacent clothing.

DISCUSSION

DR. BROWN: I think that it is a case of lipofibroma.

DR. BROCKELMANN: I believe that the tumors are too soft for lipofibroma. I think they suggest multiple lipoma.

DR. KRING: I agree with Dr. Brockelmann.

DR. CORNBLEET: The growths are in the skin, since they are freely movable together with the skin over the subcutaneous structures, but the cutis and tumors are firmly attached.

DR. GRINDON: I should diagnose them as multiple lipomas or lipofibromas, which are at times quite hard and at other times soft.

DR. TOBIAS: There is a case in the literature described by Unna, occurring in a man who later developed tuberculosis with marked loss of subcutaneous fat. The tumors, however, did not disappear nor decrease in size, thus showing their independence of the general metabolism.

DR. MOOK: These lipomas are encapsulated, they are collections of fat growing as tumors.

NORMAN TOBIAS, M.D., Secretary.

Book Reviews

REMINISCENCES. By GEORGE HENRY FOX, A.M., M.D. Cloth. Price, $3.50. Pp. 248, with illustrations. New York: Medical Life Press, 1926.

Under the modest title of "Reminiscences," which could without any supererogation be called an autobiography, Dr. George Henry Fox relates the history of a long and distinguished professional life, full of interest, especially to his dermatologic confreres. In perusing the neat and typographically elegant volume, one is reminded of the French adage: "The appetite comes with the eating." Here the pleasure comes with the reading. When an octogenerian with such mental alacrity and youthful humor records past events so interestingly, one is bound "to sit up and take notice." One lives in deeds and not in years.

He devotes the first chapter largely to the memory of his father. He relates with touching filial affection his father's fine qualities and religious sentiments.

George Henry Fox was born in October, 1846, at Balston Spa, Saratoga County, N. Y. After attending school he went to the University of Rochester, N. Y., in 1863 and graduated in 1867. As a sophomore he left college for two terms to enlist in the army during the Civil War, in which three of his brothers joined him. There is a hereditary proclivity of active patriotism running through the family as well as a peculiar inherent adaptation for the medical profession. His father was a soldier in the War of 1812, his grandfather had been a soldier in the Revolution, and his great grandfather fought in the Colonial Wars. Four of the grandsons and three of the great grandsons—one of whom is Dr. Howard Fox, the son of George Henry Fox—were all officers in the late World War. It is worthy of note that from the sixth generation in ascendency up to the present there have been eighteen members of the Fox family in the medical profession.

Dr. Fox matriculated in the University of Pennsylvania in 1867 and there, as later in Vienna, Paris and London, he was fortunate to find a corps of teachers whose names are perpetuated in American and European medical history. He studied under Joseph Leidy, Alfred and Charles Stillé, R. A. F. Penrose, Hayes Agnew, Horatio C. Wood, William Pepper and others. Dr. Fox draws excellent, vivid and humorous sketches of the merits and peculiarities of these men and of conditions at that time which are of historical value. In 1869, he entered the Philadelphia (Blockley) Hospital. After completing his internship there, he realized the ambition of most physicians to pursue their medical studies in Europe. Before settling down to it he satisfied his wanderlust by visiting Italy, Greece and Turkey. His experiences there are recorded with an often side splitting humor. Returning to Vienna in 1871 he at once settled down for serious studies. The University of Vienna at that time had its greatest medical faculty of teachers, never since surpassed —an array of brilliant men. The reviewer had the good fortune to know them all: Hyrtl, Rokitansky, Skoda, Braun, Arlt, Pollitzer, Sigmund, Zeissl and especially Hebra. Hebra must have greatly influenced Fox in his selection of dermatology as his life's study. He relates many amusing stories of Hebra, his keenness of observation and simple methods of teaching.

In Paris he studied under Bazin, Hardy and Vidal, all brilliant men in dermatology. Fox states that the method of teaching was more theoretical than practical, but withal profitable. In the spring of 1873 he went to London, frequenting various dermatologic clinics, and came in contact with Tilbury Fox, his namesake, and of "Impetigo Contagiosa" fame. There he met Dr. Henry G. Piffard who later became his most intimate friend in New York and to whose memory he devotes a chapter. He also had the good fortune to meet there Dr. Radcliffe Crocker and Sir William Osler.

To those who knew these masters personally or through their contributions to dermatology, Fox's reminiscences reflect a pleasant and instructive chapter of the makers of dermatology in Europe in the second half of the last century.

Shortly after his return to New York in 1873 Fox devoted his entire attention to diseases of the skin. He went smilingly through the vicissitudes of the beginner with its unremunerative but instructive dispensary practice. He soon became an active member of the New York County and State Medical Society, and later he was president of both. In 1873 he was made a member of the New York Dermatological Society, the oldest dermatologic society in the world. Its muster roll bears the names of Bumstead, Otis, Taylor, Piffard, Morros, Jackson and others whose scientific contributions will outlive them and perpetuate their memories. Advance came quickly to the hard working Fox, and in 1884 he was appointed to the professorship in dermatology of the College of Physicians and Surgeons in New York, which he held for thirty years. He was one of the six men who planned and organized the American Dermatological Association in 1876. As recently as in May, 1926, he delivered the Golden Anniversary address of the association at its semicentennial session in Philadelphia. Fox relates many amusing incidents of his professional life in New York. It seems that a delicate sense of modesty retarded his facile pen from giving us more of it, but what he says opens an interesting vista of New York dermatologic life, both scientific and social.

Dr. Fox gives us a highly enjoyable history of himself and his contemporaries, and a glimpse of American dermatology during the latter half of the last century. An easy flowing, cheerful and amusing style adds zest to its reading. The pages are replete with anecdotes and amusing incidents. While the long span of his happy and industrious life was mainly devoted to dermatology, as teacher, author and practitioner, he in recent years developed a hobby for geneology, especially that of his family.

He published many photographic atlases on skin diseases and syphilis, which are well known to the profession.

Those of us who have the privilege of knowing him personally can almost hear his voice and its peculiar but pleasant intonation throughout the reading of the book. Fox is not only a well liked physician but also a companionable man, a true friend and a convivial amiable fellow who takes life's enjoyments as a recompense from serious work, well balanced in all its activities. His book will be welcome and amusing reading to every one who likes to be lifted out of the everyday grind mill, and one will finish it with regrets that continuation is neither promised nor in view.

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